VOLUME 80 • SEPTEMBER 1959 • NUMBER 3

A.M.A. ARCHIVES OF

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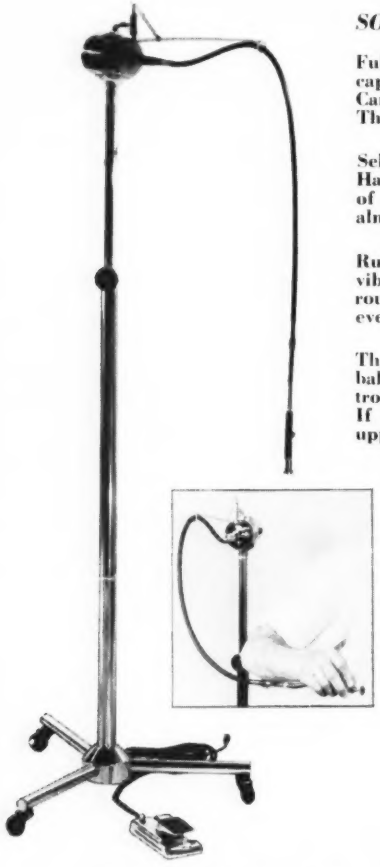

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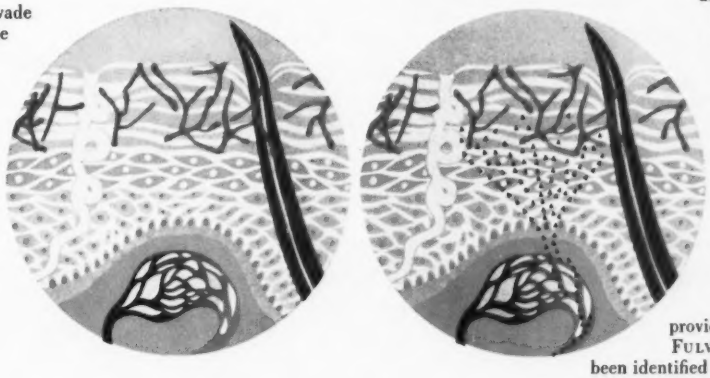

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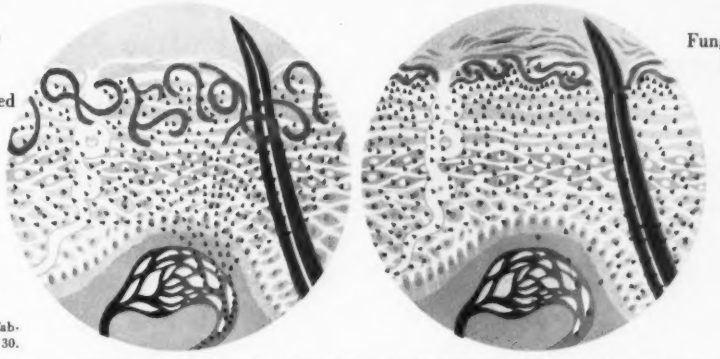

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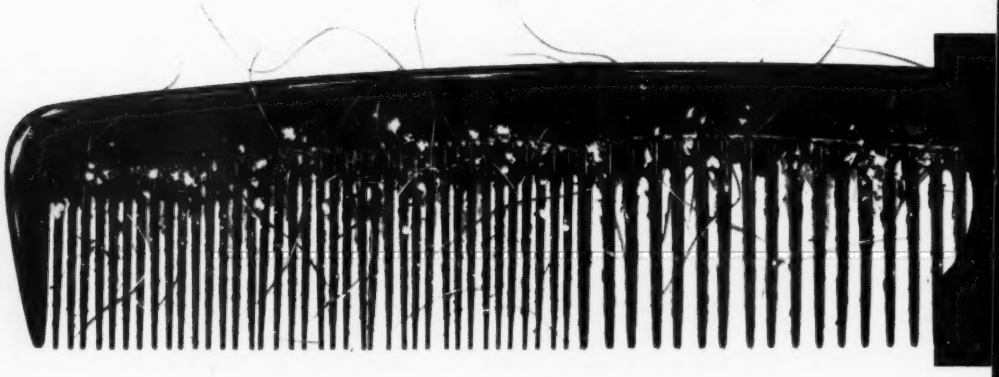

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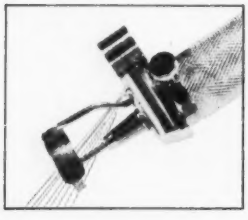

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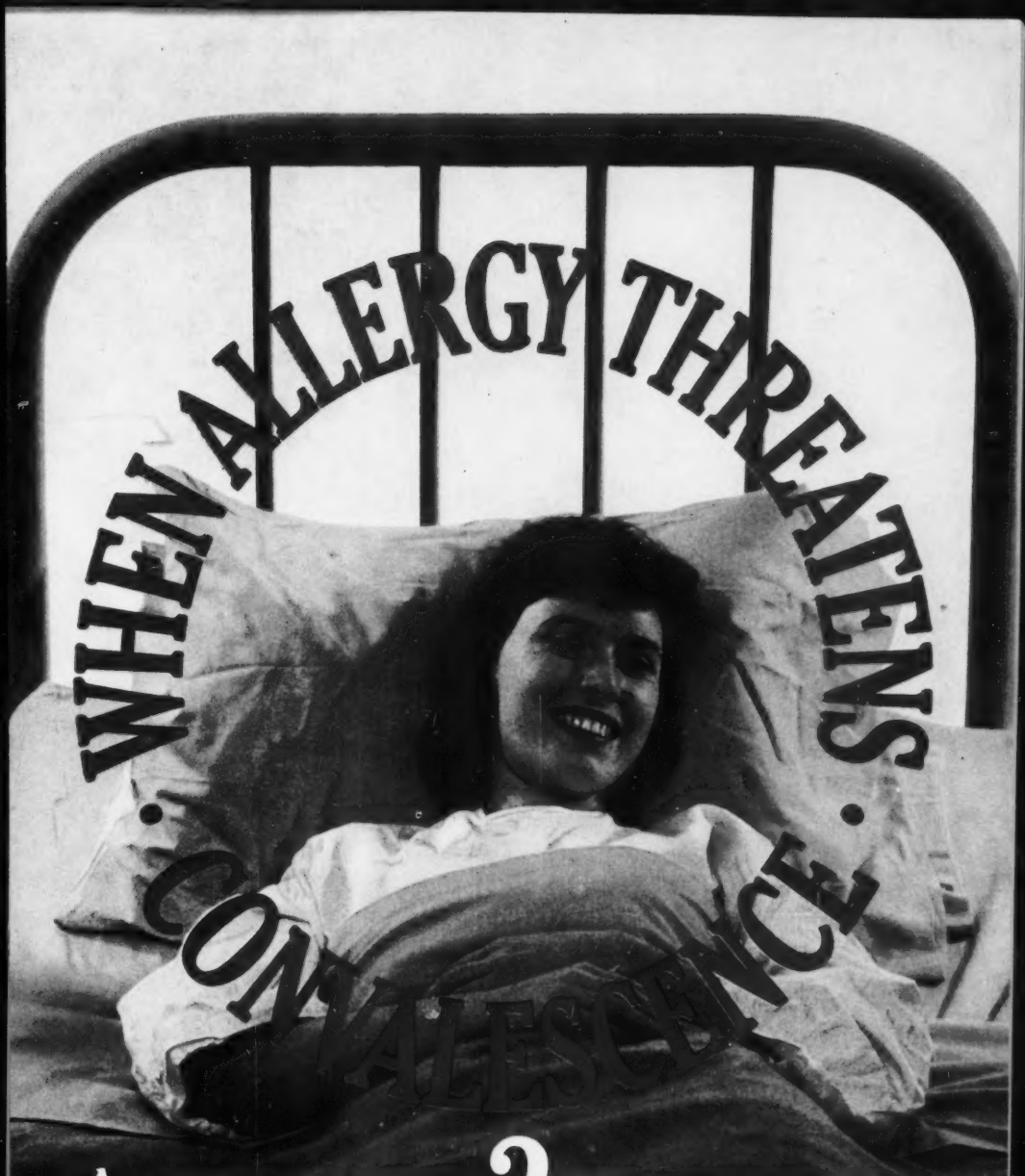

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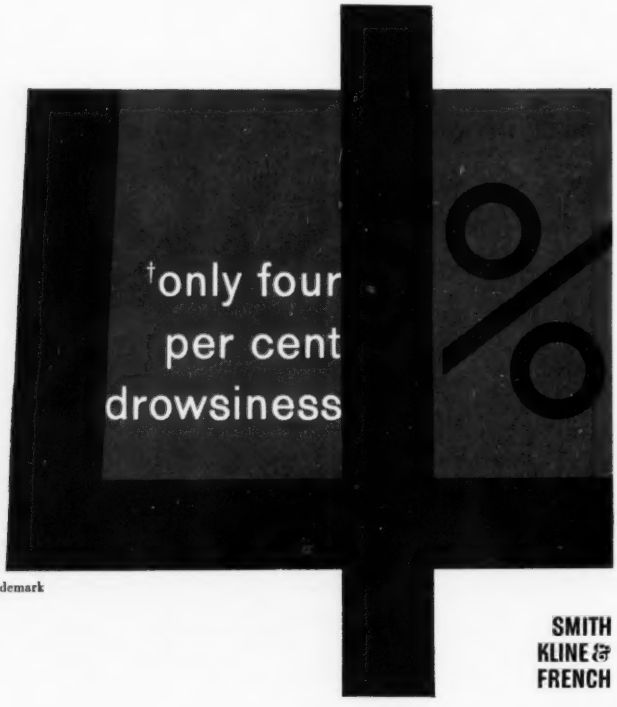

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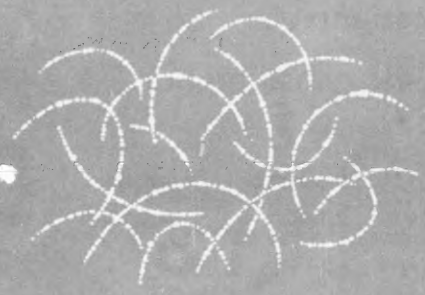

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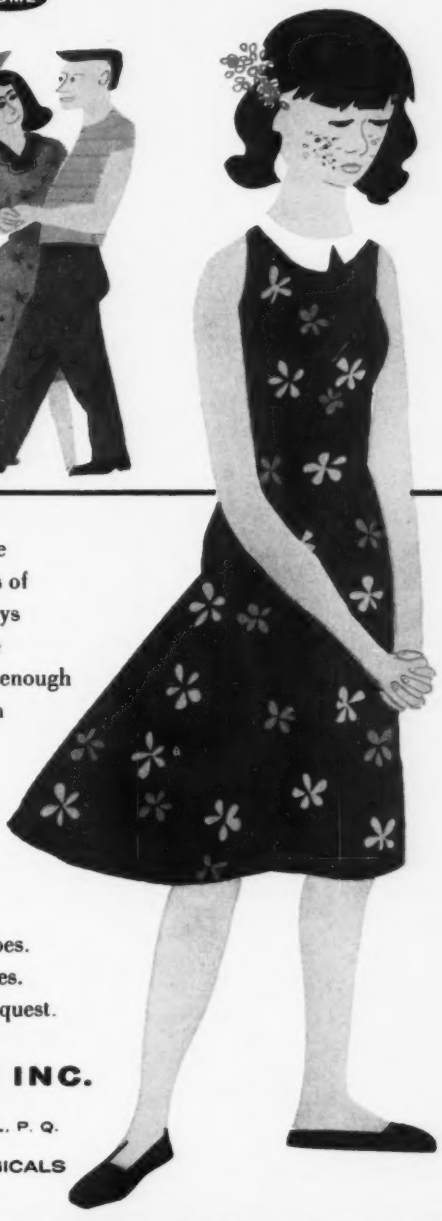

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In two clinical studies[1-2] comprising 41 patients, *all* dermatomycoses caused by any species of *Trichophyton, Microsporum* or *Epidermophyton* showed a uniformly favorable response to GRIFULVIN. Patients found rapid relief from itching; infected palms soon lost their hyperkeratosis; normal sweating, long absent, returned; normal growth replaced infected nails, and scalp lesions disappeared in two weeks. Subjective complaints by patients were few and mild.

See professional literature for details of administration and dosage.

Supplied: 250 mg. scored, aquamarine tablets, imprinted McNEIL, bottles of 16.

(1) Williams, D. I.; Marten, R. H., and Sarkany, I.: Lancet 2:1212 (Dec. 6) 1958. (2) Blank, H., and Roth, F. J., Jr.: A.M.A. Arch. Dermat. *79*:259, 1959. (3) Goldfarb, N., and Rosenthal, S. A.: Current M. Digest *26*:99, 1959. (4) Wrong, N. M.: Canad. M. A. J. *80*:656 (April 15) 1959.

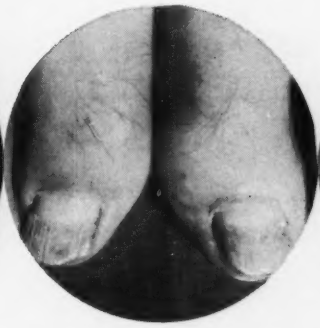
McNEIL

McNEIL LABORATORIES, INC • PHILADELPHIA 32, PA.

24939

DRAMATIC IMPROVEMENT IN TRADITIONALLY REFRACTORY RINGWORM INFECTIONS

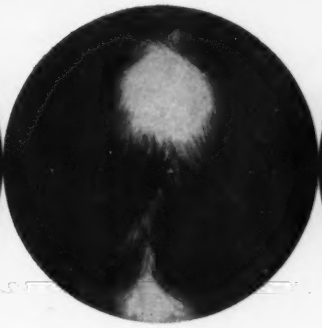
T. rubrum infection of 7 years' duration.



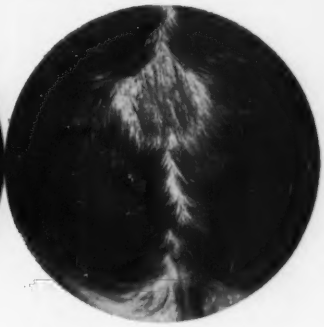
After 4 months of treatment with GRIFULVIN.

Same patient after 6 months of treatment with GRIFULVIN.

M. canis infection of 6 months' duration.

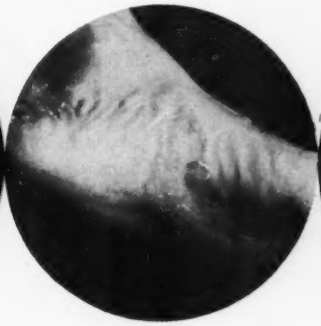


Before treatment.



Three months after therapy with GRIFULVIN.

T. rubrum infection of 20 years' duration.



Before treatment.

After 1 month of treatment with GRIFULVIN.

The patients shown above received GRIFULVIN brand of griseofulvin. Photographs by courtesy of Harvey Blank, M.D.; Miami, Fla.

normal protective cover

Normal skin has an acid pH range between 4 and 6

Samples and literature on request

Supply:
ACID MANTLE Creme: 1 oz. tubes, 4 oz. & 16 oz. jars.
ACID MANTLE Lotion: 1 oz. and 4 oz. squeeze bottles, 1 pint bottles.

ACID MANTLE®

CREME or LOTION pH 4.2

In housewives' eczema and industrial dermatitis, promptly restores and maintains the normal protective acidity of the skin. Active ingredient is aluminum acetate in specially formulated bases.

"The importance of a measure designed to return the pH of the skin quickly to its normal values after exposure to soap and alkalies is amply borne out..."

—Gross, P., et al.: A. M. A. Arch. Dermat. & Syph. 70:94,1954.

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A MUST IN DERMATOLOGY

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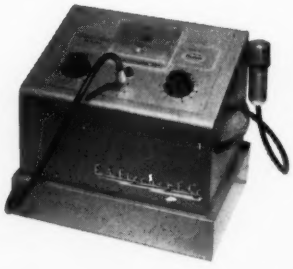
Model No. 88
Fischer Dry Pads For Low Volt
No Moisture * Send For Details

A MUST IN DEPENDABLE

ULTRA SOUND



RF-7 Ultra Sound with new 6 or 12 foot very thin, flexible low volt cables.

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Skin deep or deeper?

Certain skin disorders are due primarily to "nerves", others are often aggravated by anxiety, tension, and fear.[1]

'Miltown' therapy, 400 mg. t.i.d., relaxes the mind and allays somatic symptoms of anxiety and tension. It was used with encouraging results in a series of 164 patients with inflammatory skin conditions, including atopic, eczematoid and neurodermatitis, lichen planus, psoriasis, and anogenital pruritus.[2]

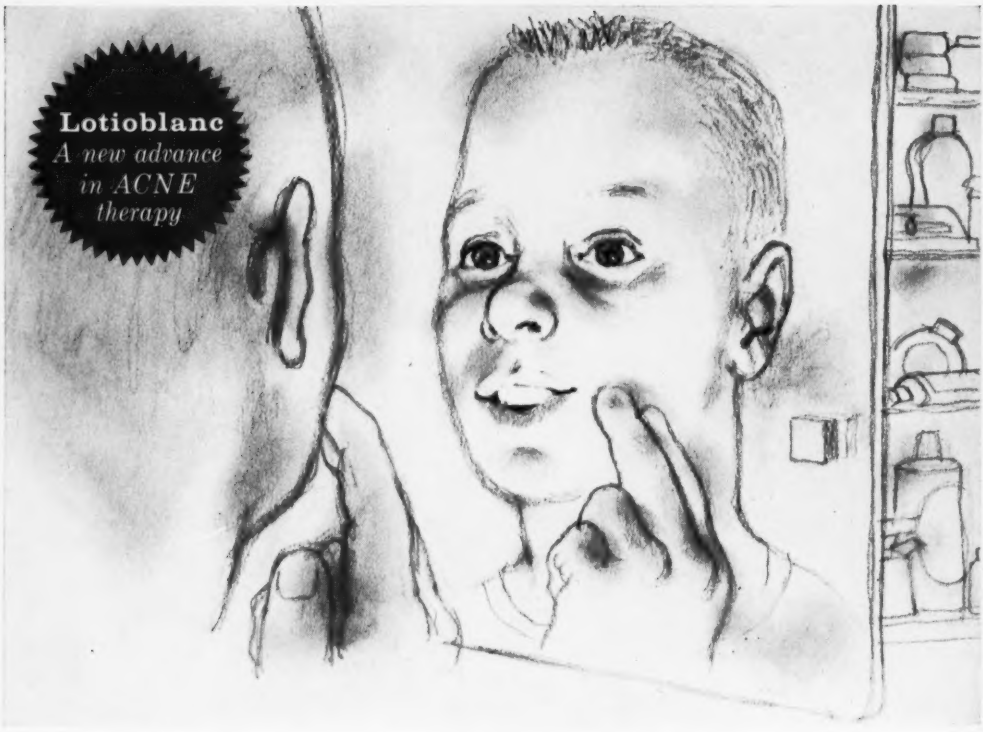
'Miltown' has been found "an effective addition to conventional dermatological therapy."[3] Results were achieved "without impairment of physical activity or mental alertness."[3]

References: 1. *Cahn, M. M.: The use of tranquilizing drugs in dermatology. J. Albert Einstein M. Center* **4**:*161, Sept. 1956.*
2. *LeVan, P. and Wright, E. T.: Use of tranquilizers in diseases of the skin – A preliminary report. California Med.* **85**:*87, Aug. 1956.*
3. *Sokoloff, O. J.: Meprobamate (Miltown) as adjunct in treatment of anogenital pruritus. A.M.A. Arch. Dermat. & Syph.* **74**:*393, Oct. 1956.*

Miltown®

meprobamate (Wallace)

WALLACE LABORATORIES, *New Brunswick, N. J.*



You can see the results, but not the medication

New stabilized lotion

Lotioblanc is a new stabilized form of traditionally effective medicaments in an improved colloidal vehicle. Prepared with Zinc Sulfate and Sulfurated Potash according to the method of the U.S.P. and improved through the addition of physiologically inert stabilizing agents. This provides uniform colloidal dispersion. The stability of Lotioblanc gives enhanced therapeutic effectiveness, and the absence of insoluble settling means uniformity of application, with minimal incidence of skin irritation.

- *Can neither be seen nor felt on the skin*
- *Permits continuous 24-hour treatment*
- *Will not stain clothing or linens*
- *No sulfur odor*
- *Greaseless*

Patient acceptance

From the patient point of view, Lotioblanc is easy and pleasant to use for both male and female patients. After application, it can not be seen nor felt on the skin, an important advantage to patients who are embarrassed by visible acne medication. Can be used with usual cosmetics. Allow Lotioblanc to dry before applying rouge or powder.

Composition:

Zinc Sulfate	40 Gm.
Sulfurated Potash	40 Gm.
Inert aqueous vehicle, q. s.	1000 cc.

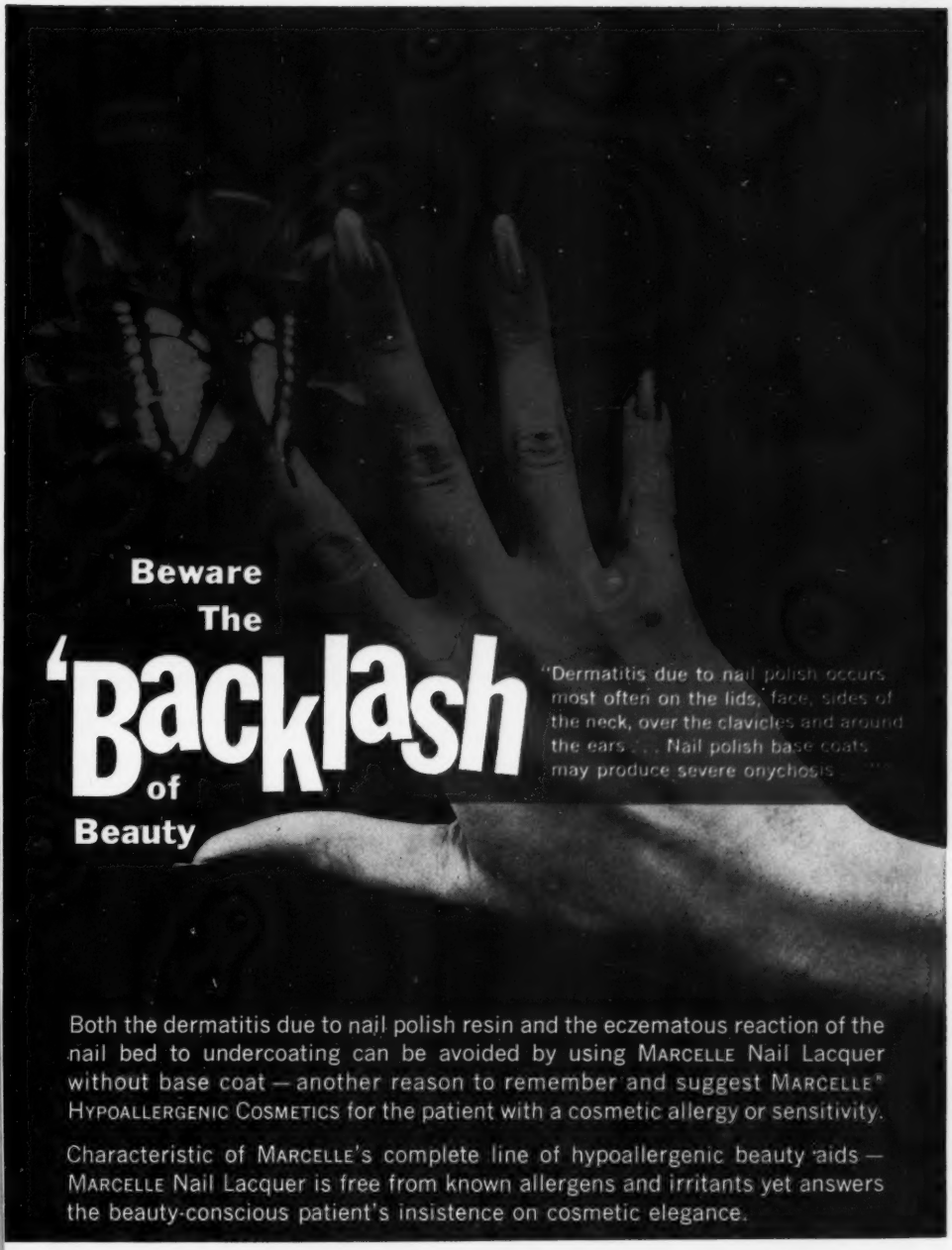
Available:

4 Fl. Oz. bottles
Write for Clinical Supply

A new advance in ACNE therapy

Lotioblanc®

ARNAR-STONE LABORATORIES INC. / MOUNT PROSPECT, ILLINOIS


Beware
The
'Backlash
of
Beauty
"Dermatitis due to nail polish occurs most often on the lids, face, sides of the neck, over the clavicles and around the ears . . . Nail polish base coats may produce severe onychosis"

Both the dermatitis due to nail polish resin and the eczematous reaction of the nail bed to undercoating can be avoided by using MARCELLE Nail Lacquer without base coat — another reason to remember and suggest MARCELLE* HYPOALLERGENIC COSMETICS for the patient with a cosmetic allergy or sensitivity.

Characteristic of MARCELLE's complete line of hypoallergenic beauty aids — MARCELLE Nail Lacquer is free from known allergens and irritants yet answers the beauty-conscious patient's insistence on cosmetic elegance.

Marcelle COSMETICS

Borden's PHARMACEUTICAL DIVISION
350 Madison Avenue, New York 17

Available in Canada through Prof. Sales Corp., Montreal

*Andrews, G. C.: Diseases of the Skin, ed. 4, Philadelphia, Saunders, 1954, pp. 117, 118

No longer *itched*

bothered or

bewildered

Pruritus is relieved rapidly and erythema and lichenification of the skin are reduced within a short period after initial application of NEO-CORT-DOME. Secondary infection is controlled and the normal pH of the skin and external auditory canal is restored and maintained with NEO-CORT-DOME.

FOR INFECTIOUS DERMATOSES AND OTITIS EXTERNA

NEO-CORT-DOME™

CREME AND LOTION pH 4.6

DOME

Hydrocortisone—Neomycin—In Aluminum Acetate Vehicle

INCORPORATED IN EXCLUSIVE ACID MANTLE® VEHICLE

Note: Lotion is especially effective in hairy areas and in tissue folds. *Supply:* ½% or 1% hydrocortisone, with 5 mg. per gm. Neomycin Sulfate in ½ oz., 1 oz., 4 oz. squeeze bottles. (½ oz. size has special soft plastic tip for easy application into external ear in otitis externa). *Sample* and literature available on request.

DOME CHEMICALS INC.
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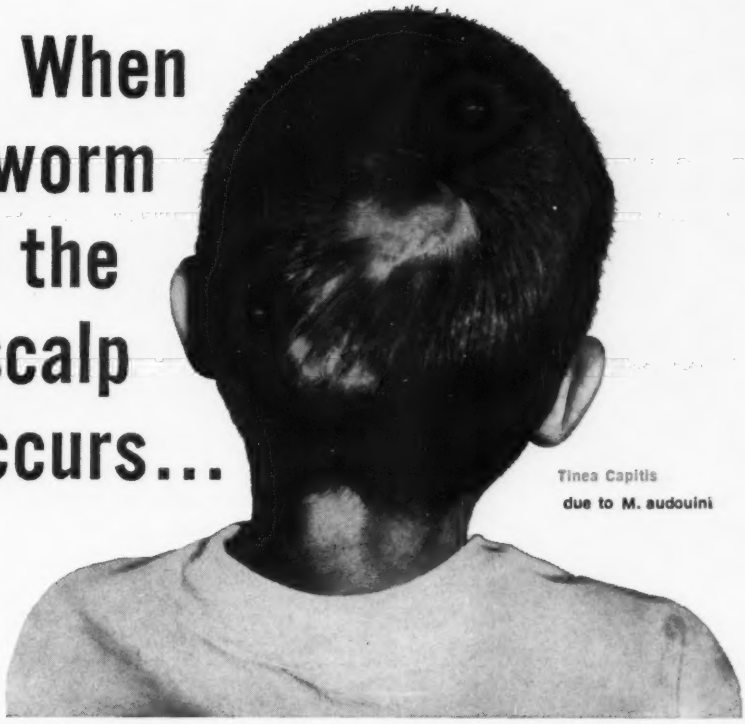
When ringworm of the scalp occurs...



Tinea Capitis
due to M. audouini

. . . topical antifungal therapy is recommended as immediate treatment. Prompt use of Salundek will destroy accessible spores and form a protective coating, reducing the likelihood of spread of the disease to other areas of the scalp, or to other children.

*New Dosage Form, Salundek Solution** – It is supplied in 3-ounce bottles with a controlled flow applicator cap. Now there is a choice that will lead to better patient cooperation during the treatment of this stubborn disease.

Many investigators have reported that the ointment and the solution have the same high percentage of cures, obtained in an average of 12 to 16 weeks.

Salundek also eliminates the hazard of x-ray therapy • seldom causes skin reaction • offers convenience in use – no stain, no odor and no effect on future hair growth.

Supplied: SALUNDEK OINTMENT, 2 oz. tubes and 1 lb. jars. SALUNDEK SOLUTION, 3 oz. bottles with controlled flow applicator cap.

Write for supply of "Instructions for Home Care" pads.

SALUNDEK®

(Brand of Zinchlorundesal)

OINTMENT
SOLUTION

Maltbie

MALTBIE LABORATORIES DIVISION • Wallace & Tiernan Incorporated • Belleville 9, N. J.

*In the presence of open lesions, the use of the ointment may be preferred at first since the base of the solution causes occasional transient stinging. Avoid contact with the eyes.

The improved, new local anesthetic. What's the new, highly efficient local anesthetic for minor surgical procedures? Many physicians say it's Gebauer's new Fluro-Ethyl. An actual report: "I have used your mixture of 25% Ethyl Chloride and 75% "Freon" for skin planing and I find it most efficient for my purposes. Freezing is fast, each container lasts a long time, results are highly satisfactory".

Equally useful as a local anesthetic for incision of furuncles, electrocautery to small cutaneous tags, flat warts, nevi, and alleviation of needle pain in hypodermic injection. Non-flammable, requires no blower. Compare Fluro-Ethyl with the product you have been using. Gebauer Chemical Company, 9410 St. Catherine Avenue, Cleveland 4, Ohio.

① Gebauer's Ethyl Chloride in new Dispenseal amber glass. ② Metal tube for doctor's emergency kit. ③ Fluro-Ethyl in the aerosol container.

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TO TREAT

ITCHY, SCALY SCALP

WHICH TENDS TO DRYNESS

sebulex®

ANTISEBORRHEIC SHAMPOO

WESTWOOD PHARMACEUTICALS, Buffalo 13, New York

sebulex®

a therapeutic shampoo
for the treatment of itchy, scaly scalp
which tends to dryness

Stops itching, removes loose dandruff and crusty, matted layers of scales from the scalp through the effective cleansing, penetrating and antiseborrheic actions of *Sebulytic*®, a combination of anionic surface-active cleansers and wetting agents. The antiseborrheic qualities of Sebulytic are further enhanced with the addition of sulfur and salicylic acid. Hexachlorophene provides antibacterial action.

Prevents excessive drying of the scalp through the action of *Kerohydric*™, a crystal-clear, dewaxed fraction derived from lanolin. Kerohydric also leaves the hair soft and more manageable after shampooing.

Sebulex is cosmetically elegant. Sebulex meets the up-to-date "cosmetic" requirements for a therapeutic shampoo. It has a smooth, lotion-like texture, an appealing pastel green color, delightful fragrance and produces an abundant lather. Patients like shampooing with Sebulex.

Sebulex does not contain any toxic metallic materials. Thus, it can be used for a prolonged period of time without danger of systemic toxic effects.

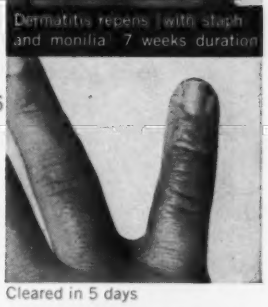
Sebulex contains a mixture of anionic surface-active cleansers and wetting agents (Sebulytic). These agents consist of sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate, and sodium dioctyl sulfosuccinate. Sebulex also contains Kerohydric, a crystal-clear, dewaxed fraction of lanolin; sulfur 2%, salicylic acid 2% and hexachlorophene 1%.

Available: In plastic bottles of 4 oz. *Write for samples.*

WESTWOOD PHARMACEUTICALS, Buffalo 13, New York

new for total management of itching,[1,2] inflamed,[3,4] infected[5,6] skin lesions

Dermatitis repens [with staph and monilia] 7 weeks duration

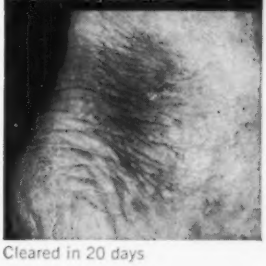


Cleared in 5 days

Mycolog ointment

Kenalog, Spectrocin and Mycostatin in Plastibase

Infectious eczematoid dermatitis of ankle—5 years duration



Cleared in 20 days

antipruritic/anti-inflammatory/antibacterial/antifungal

Mycolog Ointment – containing a new superior topical corticoid Kenalog – reduces inflammation,[3,4] relieves itching,[1,2] and combats or prevents bacterial, monilial and mixed infections.[5-7] It is extremely well tolerated, and assures a rapid, decisive clinical response for most infected dermatoses.

> **"Thirty-one of 38 patients . . . obtained excellent or good control of dermatological lesions . . . [Mycolog] was highly effective, particularly in the management of mixed infections. Several recalcitrant eruptions which had not responded to previous therapy were remarkably responsive to the daily application of this preparation over periods of 2 to 3 weeks."[5]**

For total management of itching, inflamed, infected skin lesions, Mycolog contains triamcinolone acetonide, an outstanding new topical corticoid for prompt, effective relief of itching, burning and inflammation[1-4] – neomycin and gramicidin for powerful antibacterial action[7] – and nystatin for treating or preventing Candida (Monilia) albicans infections.[8,9]

Application: Apply 2 to 3 times daily. Supply: 5 Gm. and 15 Gm. tubes. Each gram supplies 1.0 mg. (0.1%) triamcinolone acetonide, 2.5 mg. neomycin base, 0.25 mg. gramicidin, and 100,000 units nystatin in PLASTIBASE.

References: 1. Shelmire, J.B., Jr.: Monographs on Therapy 3:164 (Nov.) 1958. • 2. Nix, T.E., Jr., and Derbes, V.J.: Monographs on Therapy 3:122 (Nov.) 1958. • 3. Robinson, R.C.V.: Bull. School of Med., U. Maryland 43:54 (July) 1958. • 4. Sternberg, T.H., Newcomer, V.D., and Reisner, R.M.: Monographs on Therapy 3:115 (Nov.) 1958. • 5. Clark, R.F., and Hallett, J.J.: Monographs on Therapy 3:153 (Nov.) 1958. • 6. Smith J.G., Jr., Zawacki, R.J., and Blank, H.: Monographs on Therapy 3:111 (Nov.) 1958. • 7. Monographs on Therapy 3:137 (Nov.) 1958. • 8. Howell, C.M., Jr.: North Carolina M.J. 19:449 (Oct.) 1958. • 9. Bereston, E.S.: South. M.J. 50:547 (April) 1957.

And whatever the topical corticoid need, a suitable Squibb formulation is available—Kenalog-5 Lotion—7½ cc. plastic squeeze bottles. Each cc. supplies 1.0 mg. (0.1%) triamcinolone acetonide, 2.5 mg. neomycin base and 0.25 mg. gramicidin. Kenalog Cream, 0.1%—5 Gm. and 15 Gm. tubes. Kenalog Lotion, 0.1%—15 cc. plastic squeeze bottles. Kenalog Ointment, 0.1%—5 Gm. and 15 Gm. tubes.

SQUIBB

Squibb Quality — the Priceless Ingredient

"SPECTROCIN"®, "MYCOSTATIN"®, "PLASTIBASE"®, "MYCOLOG" AND "KENALOG" ARE SQUIBB TRADEMARKS

Adolescence can be almost unbearable to the boy or girl with acne. And, unfortunately, the self-consciousness and embarrassment that accompany acne do not always disappear when the acne is controlled. These emotional scars too often remain.

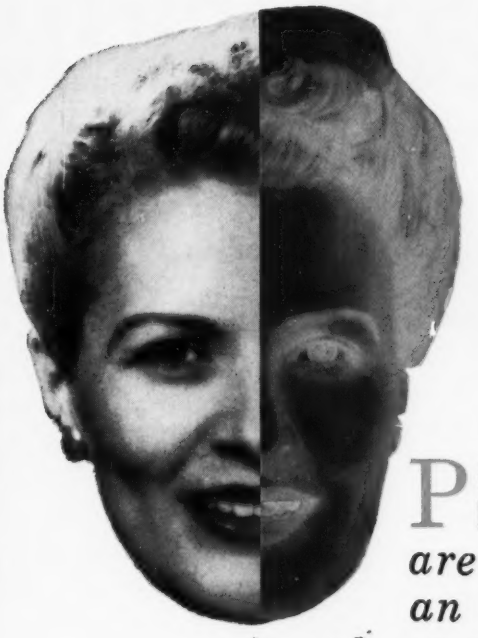
Many of the acne cases you see will respond to treatment with 'Acnomel'. Improvement is often apparent in a matter of days, rather than in weeks or months.

Flesh-tinted 'Acnomel' conceals acne pimples and lesions as it heals them. Its special vehicle makes 'Acnomel' nonstaining, easy to apply and to remove. And Acnomel's three proven ingredients—sulfur to reduce sebaceous secretion, resorcinol to dry the skin and expel keratin, and hexachlorophene to control bacterial infection—assure excellent topical treatment for acne.

'Acnomel' is available in both Cream and Cake form: Cream for use at home, and Cake (in a handy compact) for use away from home. Used together, 'Acnomel' Cream and Cake provide effective, convenient 24-hour therapy.

Acnomel® conceals as it heals

SKF *Smith Kline & French Laboratories, Philadelphia*



PSORIATICS

are half personalities, for an uncomfortable person is only one half a personality

EPIDOL®

will help to restore the psoriatics' appearance and self-confidence.

EPIDOL is a clear, *adhesive, non-greasy,* rapidly drying, improved Wright Liquor Carbonis Detergens plus Salicylic Acid 3%.

EASY to apply. Applicator comes with every bottle.

EASY to remove. Readily washes off with soap and water.

Discover how rapidly and effective EPIDOL may relieve the discomfort and clear the lesions. It helps restore the patient's feeling of comfort. Your psoriatic patients may, once again, become confident, full personalities.

SUPPLIED: Bottles with applicators: 3 fl. oz.—6 fl. oz.

Samples, literature and reprints are available. Just write to:

Spirt & Co., Inc.
WATERBURY, CONN.

TO PROTECT SKIN

AGAINST A WIDE RANGE OF IRRITANTS

- *in industry*
- *in the home*

Silicote provides an important advance in protecting skin from dry and aqueous irritants—prophylactically to prevent skin maceration, and therapeutically to exclude water, soap, and other substances from dermatoses that may be aggravated by them.

Clinical tests show that Silicote provides excellent protection against soap and water and soluble cutting oils.[1]

The protective property of Silicote is purely mechanical. Protective efficiency is necessarily determined by the nature and frequency of exposure. Frequency of application should be adjusted to provide adequate protection with minimum dosage.

SUGGESTED DOSAGE: Cleanse area thoroughly with soap and water. Apply thin film as required and rub in well. If skin is exposed constantly to irritant, apply every 2-4 hours, or as needed to provide protection. It is not necessary to remove original coat before applying subsequent coats. Any objectionable greasiness may be removed by wiping with a dry cloth, or washing gently with soap and water.

CONTRAINDICATIONS: Do not use on weeping or infected areas.

In Housewife's Eczema
Industrial Dermatoses
Chapping—Chafing
Intertrigo
Diaper Rash
Chronic Dermatoses
Aggravated by Soap
and Water

SILICOTE CONTAINS
30% dimethicone (silicone) in a specially prepared petrolatum base. Contains no water-soluble ingredients.

Send for samples and literature

1. Shaw, J. M., and Crowe, F. W.: Skin Protective Ointments. Arch. Dermat. & Syph. 71: 379, 1955.

SILICOTE
SILICONE OINTMENT

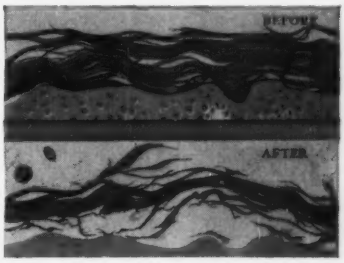
ARNAR-STONE LABORATORIES, INC. MT. PROSPECT, ILLINOIS

In Canada: Brent Laboratories, Ltd., Toronto

New freedom from embarrassment and distress of psoriasis!

Alphosyl®

LOTION



DISAGGREGATES PSORIATIC SCALE

In vitro studies show that the keratin-dispersing action of allantoin is exceptionally effective in disaggregating psoriatic scale.[1,2] It apparently acts on an abnormal cement substance between cornified cells.[2,3] Coal tar, too, helps break up the horny layer.[2] Together, these agents provide rapid clearing of psoriatic lesions as well as the underlying inflammation and erythema.

ALPHOSYL Lotion, used by many physicians both in routine practice and in carefully controlled studies, proved highly successful.[2,4-7] The lotion permits complete avoidance of the potential hazards of certain other methods of treatment, such as superficial x-ray, heavy metals and corticosteroids.[7]

Advantages: • Treatment-fastness not observed • Cosmetic qualities permit free application to the scalp • Well tolerated • May be freely used on tender areas

FORMULA: Allantoin 2% and special coal tar extract 5% in a greaseless, stainless, vanishing lotion base.

SUPPLIED: Bottles of 8 fl. oz.

APPLICATION: For maximum therapeutic results rub thoroughly into lesions 2 to 4 times daily. For maintenance apply once or twice a week.

REFERENCES: 1. Flesch, P.: Proceedings Scientific Session. Toilet Goods Assoc. June, 1958. 2. Samitz, M. H.: Ann. New York Acad. Sc. 73:1020, 1958. 3. Flesch, P., and Jackson Esoda, E. C.: Ann. New York Acad. Sc. 73:989, 1958. 4. Bleiberg, J., and Saltzman, J. A.: Clin. Med. 5:485, 1958. 5. Bleiberg, J.: Ann. New York Acad. Sc.: 73:1028, 1958. 6. Clyman, S. G.: Ann. New York Acad. Sc. 73:1032, 1958. 7. Welsh, A. L., and Ede, M.: Ohio M. J.: to be published.

For psoriasis with acute inflammation

Alphosyl-HC™

Alphosyl with 0.25% hydrocortisone
Supplied in bottles of 4 fl. oz.

R&C **REED & CARNRICK**
Jersey City 6, New Jersey

Incorporated in exclusive ACID MANTLE vehicle

Quick Soothing Topical Response

IN INFLAMMATORY DERMATOSES

Cort-Dome™

Acid Mantle-Hydrocortisone

CREME AND LOTION—pH 4.6

ABATES INFLAMMATION AND RESTORES NORMAL SKIN ACIDITY

"Susceptibility to infection by bacteria is widely held to be due to the removal of the antibacterial 'acid mantle' of the skin and its displacement by an abnormal 'alkaline mantle'."—Fabricant, N. D.: A. M. A. Arch. Otolaryn. 65:11, 1957.

Supply—⅛%, 1% and 2% hydrocortisone in either Creme (½ oz., 1 oz., 2 oz., 4 oz. tubes and 1 lb. jars) or Lotion (½ oz., 1 oz., 2 oz., 4 oz. squeeze bottles and pt. bottles).

Samples and literature available on request.

Dome Chemicals Inc.

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in urticaria and pruritus

VISTARIL* provides:

hydroxyzine pamoate

SPECIFIC ANTIHISTAMINIC EFFECT

in the treatment of a variety of skin disorders commonly seen in your practice.

"The most striking results were seen in those patients with chronic urticaria of undetermined etiology."[1]

. . . reduces—erythema, excoriation, and extent of lesions.[1-4]

PSYCHOTHERAPEUTIC POTENCY

for effective relief of tension and anxiety.[1-4]

Recommended Oral Dosage: 50 mg. q.i.d. initially; increase or decrease according to individual response.

Supplied as: Vistaril Capsules—25 mg., 50 mg. and 100 mg.

Vistaril Parenteral Solution—10 cc. vials and 2 cc. Steraject® Cartridges, each cc. contains 25 mg. hydroxyzine (as the HCl).

*Trademark

More than a tranquilizer

Science for the world's well-being

PFIZER LABORATORIES
Division, Chas. Pfizer & Co., Inc.
Brooklyn 6, New York

References: 1. Feinberg, A. R., et al.: J. Allergy *29*:358 (July) 1958. 2. Eisenberg, B. C.: Clin. Med. *5*:897-904 (July) 1958. 3. Robinson, H. M., Jr., et al.: J.A.M.A. *161*:604-606 (June 16) 1956. 4. Robinson, H. M., Jr., et al.: South. M. J. *50*:1282 (Oct.) 1957.

A NEW WIDE-SPECTRUM TOPICAL MICROBICIDE

not an antibiotic . . . not a sulfonamide . . . not a nitrofuran

Triburon

&

Triburon-HC

containing hydrocortisone 0.5%

EFFECTIVE EVEN AGAINST ANTIBIOTIC-RESISTANT STRAINS

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Ecthyma (24)	Triburon 5-14 days	excellent	none
Pustular folliculitis (16)	Triburon 1-3 weeks	infection controlled	3 complaints of burning
Dermatitis repens (18)	Triburon 1-2 weeks	infection controlled	none
Dermatitis repens (18)	Triburon-HC 1-4 weeks	excellent	none
Secondarily infected eczematous eruption (20)	Triburon 1-2 weeks	infection controlled	none
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Chart based on finding of E. Edelson, E. Grunberg and T.V. Morton Jr.

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REFERENCES: 1. R. J. Schnitzer, E. Grunberg, W. F. DeLorenzo and R. E. Bagdon, to be published.
2. E. Edelson, E. Grunberg and T. V. Morton, Jr., **Antibiotics Annual 1958-1959, New York, Medical Encyclopedia, Inc., 1959.**
3. R. C. V. Robinson and L. E. Harmon, **Antibiotics Annual 1958-1959.**

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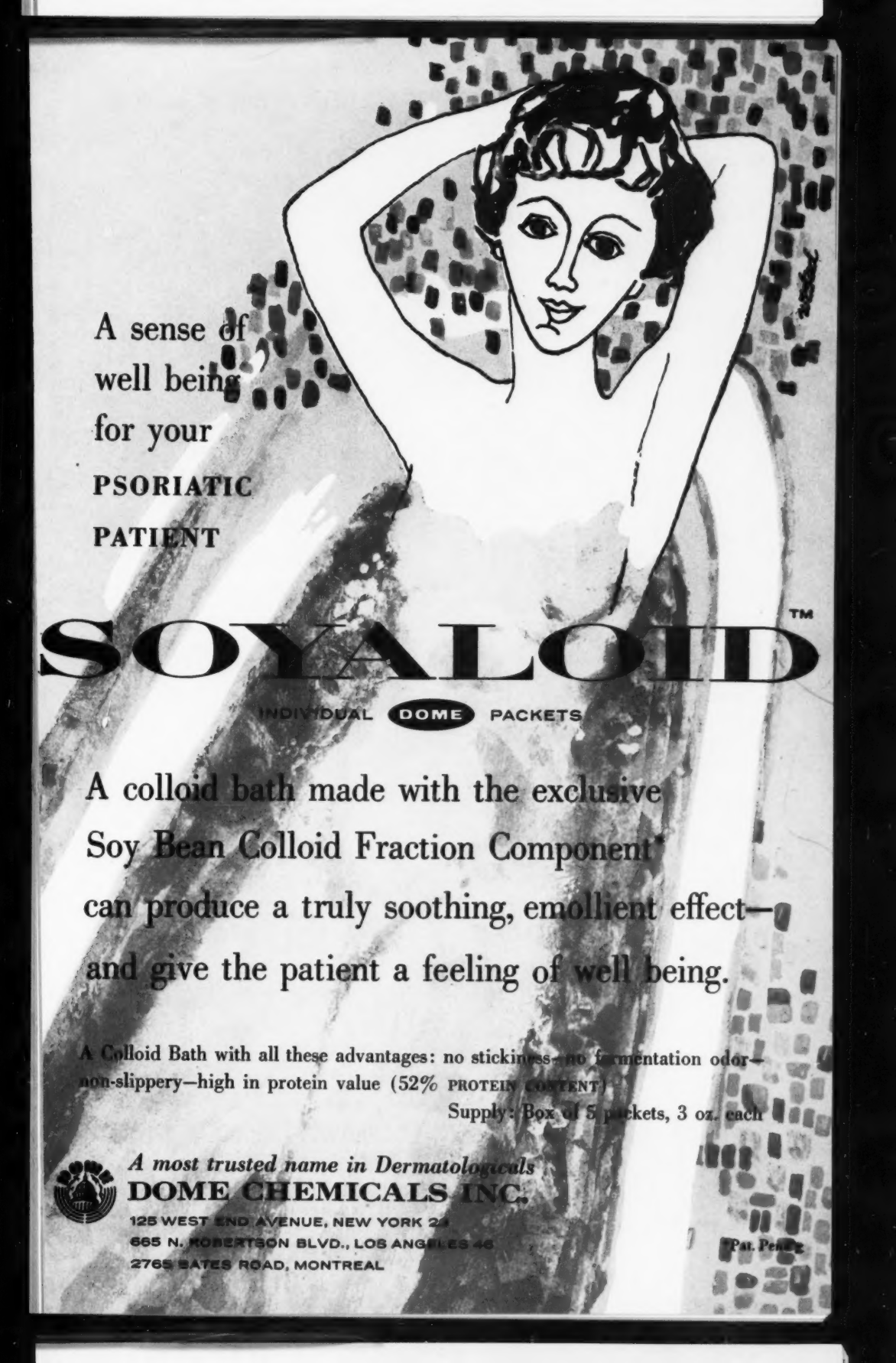
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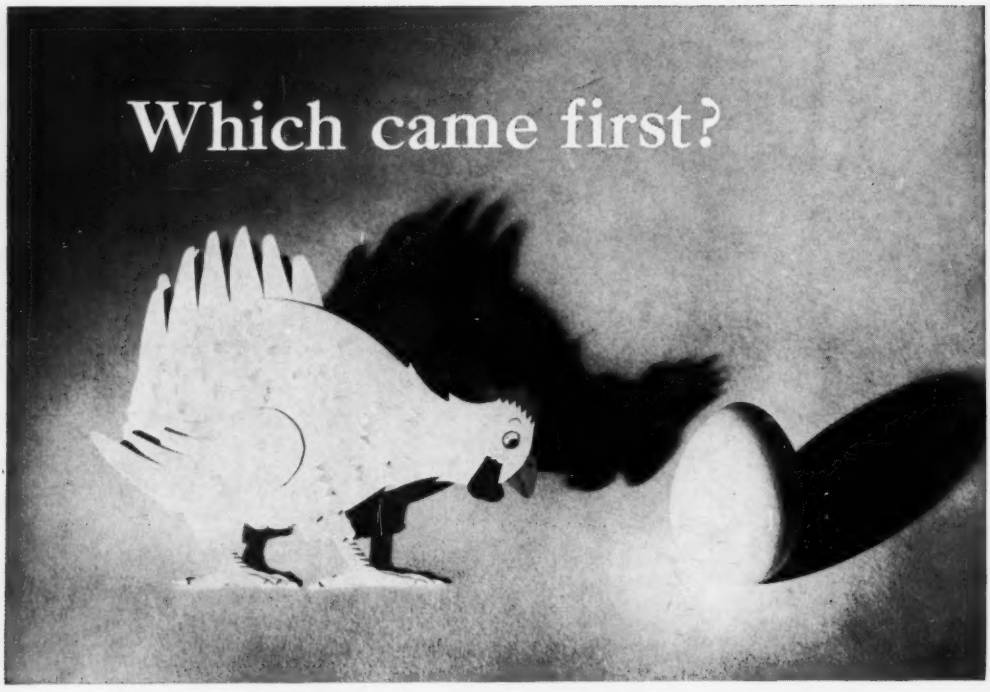

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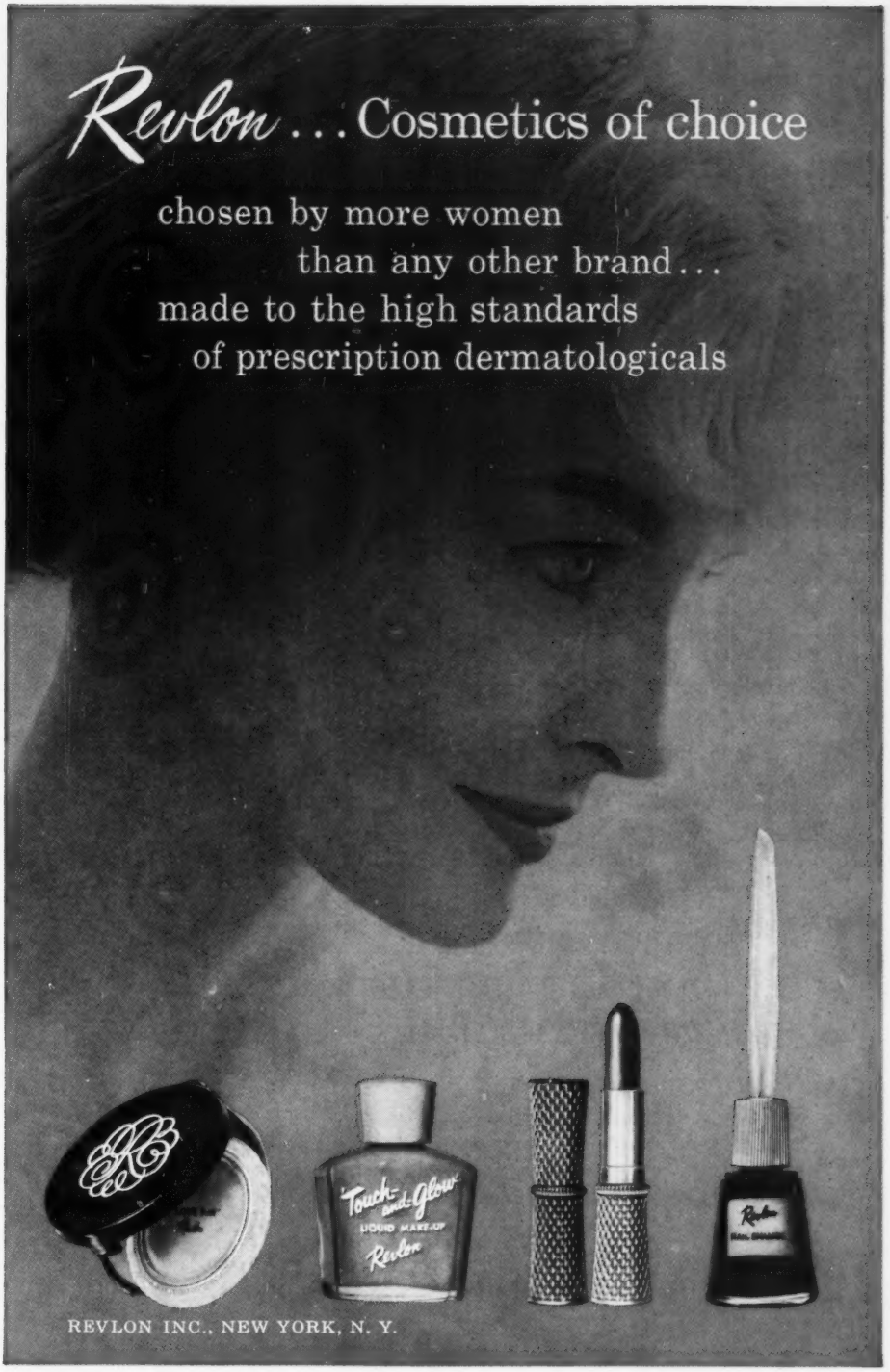
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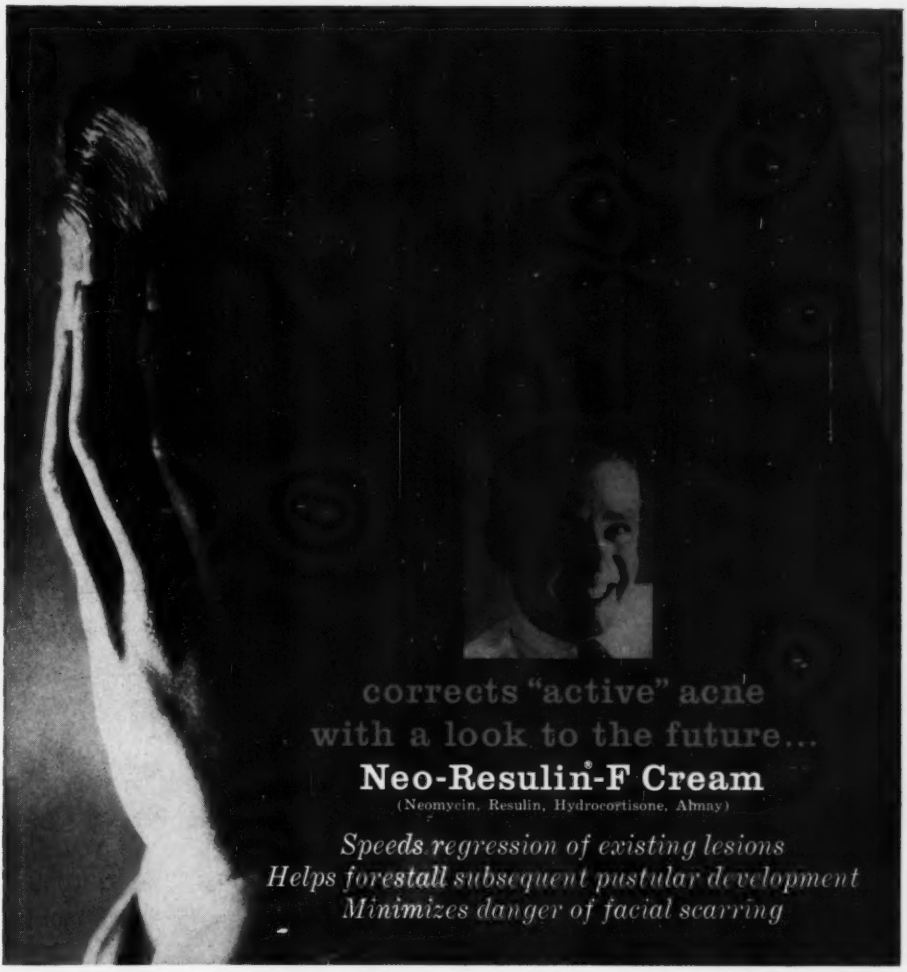
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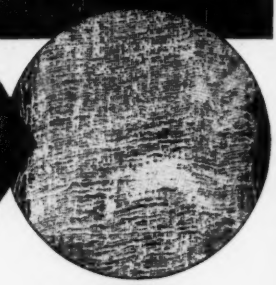

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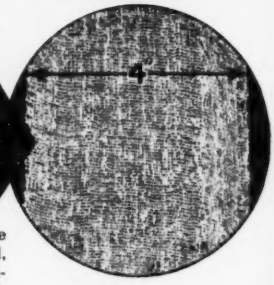

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DERMATOLOGY

Use of Griseofulvin in the Therapy of Tinea Capitis in Children

Preliminary Observations

JACQUELYN KIRK, M.D., Washington, D. C., and LIBERO AJELLO, Ph.D., Atlanta

For a number of years, the District of Columbia's Department of Public Health has been contending with tinea capitis infections among school children and their preschool siblings. From fewer than 500 new cases seen in the Ringworm Clinic of this department in the years 1949-1951, the number of new cases rose to a peak of 1,766 in 1956 (Figure).

In order to cope with this increasing problem, two and one-half years ago the Department of Public Health in consultation with the Mycology Unit of the Communicable Disease Center of the United States Public Health Service developed an intensive case-finding and systematic follow-up program. Wood's-light surveys of students in the affected schools were initiated, and suspected cases were cultured at a central clinic and confirmed cases placed under treatment and closely supervised. Thereafter, a gradually rising incidence of infection that had begun in 1951 and which had reached a total of 1,766 new cases annually by 1956 was reduced to 996 new cases in 1958. At the present time there are 656 school children under treatment for ringworm of the skin and/or scalp in the health department clinic. This figure represents approximately 0.8% of the elementary school population.

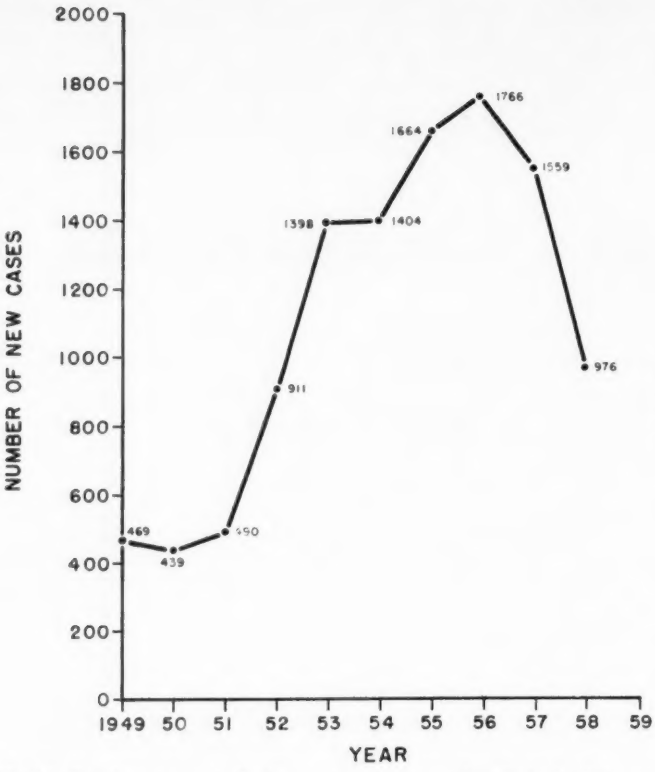
Microsporum audouini is the principal dermatophyte involved. Child-to-child transmission, chronicity, and the frequency of minimal symptoms and signs contributed to its firm establishment among the school children, particularly those from the most congested areas. This organism was isolated from 86.7% of the last 666 diagnosed cases of tinea capitis. Microsporum canis and Trichophyton tonsurans accounted for the remainder.

During the summer of 1958, a review of the M. audouini cases under topical therapy in this clinic showed that of 615 children with tinea capitis 31% had been under treatment or at least under observation for more than one year and 11% for more than two years. Cures, as determined on the basis of negative Wood's-light examination, supported by negative culture for fungi, have been rare in less than three months' time, and in those instances recovery only occurred in children who had kerion at the time of diagnosis or who developed this allergic reaction immediately thereafter.

Although x-ray therapy was known to be highly effective in the control of mycotic scalp infections, upon the advice of the Radiology Services of the U. S. Public

Submitted for publication May 15, 1959.

Department of Public Health, Bureau of Maternal and Child Health, Washington, D. C. (Dr. Kirk), and Bureau of State Services, Public Health Service, U. S. Department of Health, Education, and Welfare, Atlanta (Dr. Ajello).



Incidence of new cases of ringworm among school and preschool children in the District of Columbia from 1949 through 1958.

Health Service, x-ray epilation was not employed as a therapeutic measure by the ringworm clinic. A variety of topical preparations were used instead, but these have been disappointing in their effectiveness. Their use has been tedious, and parents as well as children have protested their unsightly nature.

After the announcement that guinea pigs experimentally infected with dermatophytes were successfully treated with orally administered griseofulvin (Gentles, 1958),[1] it was decided to test this antibiotic upon a selected group of infected children. Griseofulvin was first obtained from the Glaxo Laboratories, Ltd., Greenford, England. Subsequent supplies have been furnished by the McNeil Laboratories, Inc., Philadelphia, under the trade name of Grifulvin.* Before the clinical trials were initiated, data on the low toxicity of orally administered griseofulvin were received from Dr. Gavin Hildick-Smith, of Johnson and Johnson. Later, Dr. H. Blank, of the University of Miami School of Medicine, provided us with additional toxicity data prior to publication of his therapeutic findings.[2]

Griseofulvin was first isolated and chemically characterized by Oxford, Raistrick, and Simonart, in 1939.[3] It was described as a metabolic product obtained from the ground mycelium of Penicillium griseofulvin. In 1946, Brian, Curtis, and Hemming [4] described a fungistatic "curling-factor" isolated from Penicillium janczewski. The following year the identity of this "curling-factor" with griseofulvin was established by Grove and McGowan.[5] Subsequently, various workers discovered that this antibiotic had marked antifungal activity

* Use of trade names does not constitute endorsement by the U. S. Public Health Service or the District of Columbia Department of Public Health.

against several systemic mycotic deseases of plants.[6-8]

In view of the fungistatic properties of griseofulvin it occurred to Gentles [1] to investigate its activity through the oral route against ringworm-infected animals. A daily dose of 60 mg. per kilogram successfully cured guinea pigs experimentally infected with M. canis and Trichophyton mentagrophytes.

Material and Methods

Although 120 children have been or are now under treatment, 81 are apparently cured or have passed the 10th week of observation. Of these 81, mycologically confirmed infection with M. audouini was present in 70, with T. tonsurans in 6, and with M. canis in 5. Data regarding these therapeutic results are limited to these 81.

The patients ranged in age from 2 years to 16 years. A few had infections involving only a small number of scattered hairs, while others had 70 or more patches of fluorescent hairs. The shortest infection was of one week's duration and the longest three years, with a predominance of early cases. With the exception of two white children, all the patients were Negroes.

In order to determine the minimal effective dose of griseofulvin, a wide range of dosage schedules was tested. Because the children varied greatly in weight, dosages were calculated on a body weight basis. The lowest dosage tested was 3.1 mg. per pound per day and the highest 18.7 mg. per pound per day. However, since griseofulvin was only available in 125 and 250 mg. tablets, the amount of drug administered to the patients was rounded off to the nearest multiple or combination of the tablets.

Patients who responded satisfactorily at the lower dosage levels were maintained at these levels. Patients who developed inflammatory reactions or who showed little response after two or three weeks of therapy were given larger amounts of griseofulvin.

Early in the study it became apparent that, even with the largest doses given, a minimum of 21 to 28 days was required for the outgrowth of normal hair as observed under a 250-watt Wood's lamp. Therefore, a dosage level was sought which would result in a negative Wood's-light examination in the majority of cases within 28 days.

Complete blood cell counts and urinalyses were carried out on each patient prior to the initiation of antibiotic treatment and at weekly intervals thereafter. In the absence of side-effects, the tests are now done every two weeks.

Patients were examined at weekly intervals, and the parents were urged to shampoo their children's scalp before visiting the clinic. If scaling or crusting was present, more frequent shampoos were advised. An attempt to compare the effects of daily and weekly shampoos had to be discarded in the face of erratic parental cooperation.

Parents were requested to shave the affected areas just before the clinic visit on the 21st day of treatment, so that any persistent fluorescent hairs could be observed more readily. From this time on the hair was kept clipped or the head shaved.

Cultures with a selective isolation medium*† were made on all patients before treatment was initiated to confirm the clinical diagnosis and for species identification. Early in the study it became obvious that the green fluorescent hairs remained culture-positive, even though the patient was under treatment and the proximal end of the green fluorescent zone had grown a centimeter or more away from the scalp. Therefore, as the study progressed, after the initial culture on a given patient had been obtained, no further cultures were taken until the third to fifth week, when the fluorescent portion of all hairs could be clipped off. From this time on, culture plates were inoculated weekly to determine the presence of infectious stubs and scales.

In the earlier cases treatment was stopped as soon as the Wood's-light examination was negative in the mistaken impression that residual scales and "suspicious" yellowish-gray stubs would be quickly removed by washing or the local application of one-half strength benzoic and salicylic acid (Whitfield's) ointment. It was found that culture-positive material persisted for several weeks in some cases, and in several instances short green fluorescent hairs reappeared in the sites of previous involvement as did previously quiescent inflammatory papules and crusts. Three patients who had cleared to the stage of a single negative culture developed new lesions.

As a consequence of these experiences, treatment periods were gradually extended so that patients who entered the study later were treated until two negative cultures, taken one week apart, were obtained. The patient was then reexamined two weeks later, and scales and hair stubs were collected from the original sites of infection and cultured. One month later the patient was examined again and, if the third culture taken previously proved to be negative, he was discharged as cured.

In the T. tonsurans cases, since the infected hairs do not produce green fluorescence, the final series of culture tubes were inoculated 21 to 28 days after the initiation of therapy. At this time scaling usually had subsided and apparently normal hair had developed. Here again, three negative cultures

† Mycosel Agar, Baltimore Biological Laboratory. (Use of trade names does not constitute endorsement by the U. S. Public Health Service.)

spaced over a month to six-week period were obtained before a patient was released as cured.

Potassium hydroxide preparations were a valuable adjunct to the cultural studies, but at times the presence or absence of a few spores was difficult to determine in a given specimen. When only a few small fragments of material were available for study, only cultures were made.

Observations

Regardless of the dosage schedule, after one week of therapy, little change was observed in the infected sites. Early cases sometimes developed an extended zone of fluorescence, but this was probably due to the growth above the surface of the scalp of previously infected hairs.

At two weeks, fluorescence in some cases had faded to a fainter green. By this time the hairs were more resistant to plucking and the patients frequently complained when hair was epilated manually. Often when epilation was attempted, the tweezers slipped along the hair shaft and scraped away the fluorescent material, disclosing a faintly green hair. Close examination of the infected patient sometimes revealed a few hairs with a nonfluorescent zone approximately 1 mm. in length adjacent to the scalp.

At 21 days, the fluorescent zone of the infected hairs had grown out sufficiently to permit it to be clipped off. After this, Wood's-light examination in most cases disclosed only scattered fluorescent hairs through the previously infected patches.

After 28 days of therapy, some patients were completely Wood's-light-negative. In others, scattered faintly fluorescent hairs persisted. In certain patients, very close scrutiny disclosed the presence of very fine short grayish-yellow to white stubs which were KOH- and culture-positive.

Increased scaling over the affected areas was noted during the second and third weeks of treatment in many patients and a number of the early cases developed mild inflammatory reaction in the lesions in the form of small papules, folliculopustules and crusts. However, classical kerion developed in none.

Two patients with kerion in which griseofulvin therapy has been recently instituted have shown marked clinical improvement after only one week of treatment, with flattening of boggy, edematous areas and disappearance of exudates.

Results of Treatment

A. Microsporum Audouini Infections. Table 1 summarizes the therapeutic results obtained to date with 70 patients who are cured or who have been under observation for more than 10 weeks. For the purpose of clarity, "Wood's-light-negative" is used throughout to indicate the absence of green fluorescence and does not necessarily denote a completely normal scalp. Because of possible altered response to the drug, tabulated data do not include the second course of treatment in those patients in whom treatment was initially inadequate. Of those three patients in whom fluorescence recurred after negative cultures were obtained, all had a single negative culture at the fifth or sixth week and all recurrences were present during the ninth week after treatment was begun. Two had spontaneously dropped from treatment after two weeks, the third was taken off treatment at 21 days when the fluorescent hairs were easily clipped away. These were considered to be recurrences rather than new infections, since all had at least one lesion at a site previously involved.

Of the 16 who failed to develop consistently negative cultures by the 10th week, 9 had negative cultures beginning at 77 days, 1 at 83 days, and 1 at 95 days. The remaining five are still culture-positive at 77 days. This group includes four patients who had one or two negative cultures followed by a single positive one before becoming permanently culture-negative.

It is obvious that definitive conclusions as to optimum dosage or treatment time cannot be reached from this small series. Apparent cures have shortly followed treatment with as little as 250 mg. daily of griseofulvin for 7 to 14 days, while two patients still have

TABLE 1.—*Griseofulvin Therapy in Seventy Cases of M. Audouini Infection (Scalp)*

Dosage Schedule	Duration of Therapy	Patients, No.	Wood's-Light Examination and Laboratory Study Following Initiation of Therapy								Cultures Positive 70 Days & Longer	Treatment Failures in WL-Positive Phase	Recurrences After Culture Negative
			28 Days		42 Days		56 Days		70 Days				
			WL Negative	Culture Negative	WL Negative	Culture Negative	WL Negative	Culture Negative	WL Negative	Culture Negative			
3.1-5 mg/lb/day	Less than 28 days	5	3	1	5	3	5	3	5	5	0		1
	28 days & longer	3	1	0	3	3	3	3	3	3	0		0
5-9.8 mg/lb/day	Less than 28 days	12	5	0	9	3	9	7	9	8	1	3	2
	28 days & longer	6	4	1	5	1	5	3	5	4	1	1 treated 28 days	
10-17.4 mg/lb/day	Less than 28 days	2	1	0	2	0	2	1	2	2	0		
	28 days & longer	13	10	1	12	7	12	9	12	10	2	1 treated 28 days	
20.0-23.5 mg/lb (weekly doses)	7-10 wk.	6	3	0	6	2	6	2	6	3	3		
Combinations of above	28 days & longer	23	12 *	1	18	4	22 *	10	22	13	9	1 *	
Total		70	39	4	60	23	64	38	64	48	16	6	3

* Wood's-light-negative, culture-positive at 28 days. Recurrence of flourescence on weekly maintenance doses.

TABLE 2.—*Griseofulvin Therapy*—Effect in Thirteen Cases of M. Audouini Infection*

Case, No.	Age	Sex	Estimated Duration of Infection	Scalp Lesions, No.	Dose (Mg/Lb.)	Dosage Schedule		Weight, Lb.		Treatment Evaluation	
						Mg.	Days	Pretreatment	During or After Treatment	Wood's-Light Examination	Culture Results
4,954	4	M	5 wk.	50+	10.2	375 daily	28	36 ½	38 ½ (4 wk.)	Positive, 42 days (patient discontinued therapy at 28 days)	Positive, 42 days
4,956	4	F	1 wk.	1	13.6	375 daily	42	33	32 ½ (5 wk.)	Negative, 28 days	Negative, 28 days
4,942	5	M	3 wk.	20	12.7	500 daily	63	39 ½	40 ½ (6 wk.)	Negative, 28 days	Negative, 42 days
4,978	5	F	Indeterminate (6 mo.)	4-6 (confluent)	12.8	500 q. d.	49	39	40 (6 wk.)	Negative, 21 days	Negative, 35 days
5,038	5	F	Indeterminate (3 mo.)	4	10.6	375 daily	49	35 ½	36 (3 wk.)	Negative, 21 days	Negative, 42 days
4,973	7	F	Indeterminate (1 yr.)	1	10.1	500 daily	42	49 ½	53 (5 wk.)	Negative, 28 days	Negative, 49 days
4,806	7	M	1 wk.	2	10.5	500 daily	28	47 ½	Not recorded	Negative, 21 days	Negative, 49 days
4,703	9	M	3 wk.	9	11.8	750 daily	77+	63 ½	65 (5 wk.)	Negative, 28 days	Positive, 77 days
4,936	8	M	1 wk.	1	17.4	750 daily	35	43	43 (6 wk.)	Negative 28 days	Negative, 42 days
4,976	10	M	1 wk.	2	11.2	750 daily	49	67	66 ½ (5 wk.)	Negative, 35 days	Negative, 35 days
4,953	10	M	1 wk.	40	12.8	750 daily	77+	58 ¼	58 ½ (6 wk.)	Negative, 42 days	Positive, 77 days
1,835	11	F	21 mo. +	Scattered hairs	10.2	750 daily	35	73 ½	74 ½ (4 wk.)	Negative, 28 days	Negative, 42 days
281	13	M	29 mo. +	Scattered hairs	12.0	1,000 daily	21	83	Not recorded	Negative, 21 days	Negative, 70 days

* 10.0-17.4 mg. per pound per day. All patients infected by M. audouini.

positive cultures after 77 days of continuous therapy at 750 mg. per day.

While very good results were seen in some patients on smaller daily doses and on weekly doses, the group on "combined" dosage schedules was composed largely of patients started on small doses and gradually increased, or who were on daily therapy until the Wood's-light examination was negative and then placed on weekly maintenance doses, following which further improvement was sometimes very slow.

Even without this consideration it appears that better results have been obtained in patients who received at least 10 mg. per pound daily.

Several variables apart from griseofulvin dosage alone seemed to affect the time required for cure. Patients with tinea capitis of more than one year duration in general seemed to respond a little more rapidly than those with infections of less than two months' duration. Patients with minimal infection generally responded more rapidly than those with extensive infection. Frequent, vigorous cleansing of the scalp or the lack of it in some instances seemed to be a factor in the time required for the disappearance of fungus-bearing scales and debris after fluorescence had disappeared.

At the present time, the majority of cases entering the study are being treated with 10-15 mg. per pound per day and treatment is being maintained until at least two cultures are negative. A few have been started at 20 mg. per pound of body weight per day and others at 20 mg. per pound twice weekly. Data on therapeutic effectiveness and on side-reactions are insufficient for comparative analysis at this time.

The data in Table 2 show the treatment results in 13 patients treated with 10 mg. or more per pound of body weight per day. Since 12 of 13 patients treated on this dosage schedule for 21 to 70 days or more had negative Wood's-light examinations by the 42d day and 9 of the remaining 12 had consistently negative cultures beginning at the 56th day of treatment, it would appear that this dosage level should be adequate for cure in the majority of cases in from 8 to 10 weeks. However, the attending physician should be prepared to do fungus cultures and extend treatment beyond this point, if indicated.

To date, cases which have been treated the second time after a first, inadequate course of therapy have shown no evidence of increased drug resistance. However, patients off treatment for two weeks or more have usually required retreatment for 21 to 28 days before becoming Wood's-light-negative and further treatment before the cultures become negative.

B. Microsporum Canis and Trichophyton Tonsurans Infections.—Four patients with M. canis infection were treated with daily doses of 500-750 mg. of griseofulvin (10.6-14.5 mg. per pound) until fluorescence had disappeared, then weekly doses of 20.0-24.2 mg. per pound. All four patients were Wood's-light-negative by the 35th day. One patient was culture-negative at 56 days. Two (siblings) partially relapsed on weekly doses with the development of mild inflammation and a few fluorescent hairs in the original sites, have now been replaced on daily therapy. One was temporarily lost to follow-up after the second weekly dose; he did not become culture-negative, and when he returned to clinic five weeks later there were numerous scattered fluorescent hairs over the scalp, more widely distributed than the original sites.

One patient with M. canis infection, treated with 250 mg. daily for 42 days, was Wood's-light-negative at 35 days after the institution of therapy but showed a recurrence of fluorescence at the initial site at 49 days. Daily therapy was reinstituted immediately at 1,000 mg. (10.4 mg. per pound) and continued for 49 days. The Wood's-light examination was negative at 21 days; the culture, negative at 28 days after the second course was begun. No recurrence followed.

Six patients with T. tonsurans infection have been treated. Two patients were

treated with daily doses of 500 mg. (7.6 and 10.9 mg. per pound) of griseofulvin for 35 and 56 days, respectively; one received 250 mg. (4.7 mg. per pound) daily for 14 days, then 1,000 mg. daily for 14 days; two were given weekly doses of 1,500 mg. (21.7 mg. per pound) and 1,000 mg. (21.9 mg. per pound), respectively, for eight doses. One patient was given 500 mg. (6.9 mg. per pound) daily for 35 days, then 1,500 mg. weekly for two doses. All were clinically cured and had negative cultures by the 42d day after therapy was begun (three by the 28th day), with patients on similar dosage schedules showing the widest variations in times required for cure.

Although both the M. canis and T. tonsurans series are small, they are presented because of the difference in response to griseofulvin between these two types of infections and because of their response relationship to the M. audouini group of cases.

Side-Effects and Toxicity.—Three hundred fifty-three complete blood cell counts have been done on patients undergoing griseofulvin therapy. No evidence of bone marrow depression or renal toxicity was noted.

Weights were recorded at varying intervals and weight changes were to the order of those seen in Table 2. No significant weight losses were recorded, the majority of patients to date having shown slight but continued weight gains during and after therapy.

In two cases the tentative diagnosis of angroneurotic edema was made. In both instances the parents described "swelling about the eyes" which rapidly subsided when treatment was discontinued, only to recur within 24 hours after treatment was resumed. In neither instance was the reaction reported nor the patient brought in until the reaction had disappeared. In both instances reactions occurred during the first two weeks of therapy.

No other evidence of toxicity was reported or observed.

Summary and Conclusions

Observations in the treatment of tinea capitis in children with the antibiotic griseofulvin are reported and the results of treatment in 81 cases on varying dosages are recorded. The drug was used in infection caused by Microsporum audouini, Microsporum canis and Trichophyton tonsurans. Griseofulvin appears to be a specific agent against the invasion of newly formed hair by these fungi.

Normal hair growth may be noted in three weeks, but a few faintly green-fluorescent hairs have been present for as long as eight weeks in Microsporum infections, with fungus-bearing stubs, scales and debris remaining for as long as 95 days under continuous therapy. As the infected portion of the hair grows, this must be cut off. Consequently, clipping or shaving of the hair from affected areas is advised, beginning on or before the 21st day of treatment and should be continued until cure is obtained. Scrupulous cleanliness has seemed to facilitate the removal of infectious scales and debris.

Because of the recurrence of lesions after a single negative culture in three cases treated with low dosages and for four weeks or less, it is suggested that treatment be maintained until two cultures taken at one-week intervals are negative and that a third culture two weeks after treatment is ended be negative before the patient is discharged as cured. Wood's-light examinations should be continued for a minimum of one month after therapy is completed.

Of 13 patients with M. audouini infection treated from 28 to 70 days with dosages ranging from 10.0 to 17.4 mg. per pound per day, 10 were Wood's light negative by the 28th day of treatment and 2 by the 42d day of treatment. One patient who stopped treatment at the 28th day still had Wood's-light-fluorescent hairs two weeks later. Of this group, 10 had begun to show consistently negative cultures by the 70th day of observation, 2 remaining culture-positive after 77 days of continuous therapy.

Although M. canis and T. tonsurans infections have responded to griseofulvin therapy, the series presented are too small for conclusions as to optimum dosage. Therapy was uniformly more successful in the T. tonsurans group in the dosages used.

Out of 120 patients on griseofulvin therapy, periorbital edema in 2 cases has been the only untoward reaction noted. However, blood cell counts, urinalyses, weight changes, and clinical observations are still being made at frequent intervals.

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Melanocytic Striae in Scars and Nails

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Although pigmented striae in scars in human skin are a neglected if not unrecorded clinical finding, they can be seen regularly and are especially striking in dark-skinned persons. It is our wish to present data on the nature, origin, and significance of these microbands of pigment as seen in scars. The majority of these observations were made on the scars of Negroes in view of the ease with which the striae are viewed and studied in such patients. Over 100 such scars were studied on all areas of the body surface.

The striae are easily viewed clinically with the aid of a little magnification (× 5-20) after the application of mineral oil to the skin. Gross clinical observation of "uncleared" skin may fail to reveal their presence. Varying in color from light brown to black, the striae measure about 25μ to 75μ in width. Furthermore, they are astonishingly regular and linear. Side by side one may see scores of parallel lines

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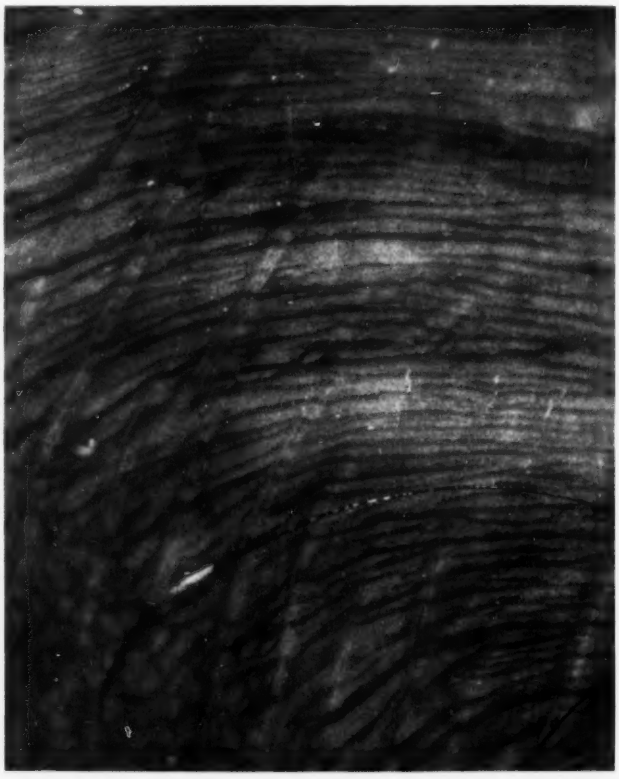


Fig. 1.—Surface view of melanocytic striae in scar. Numerous fine parallel lines of pigment are seen representing Langer's lines of tension operative in wound healing; about × 20.

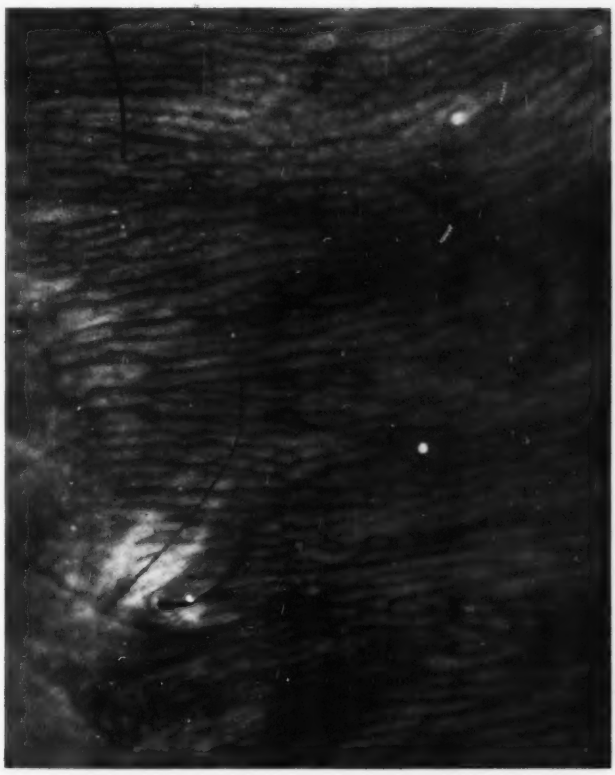


Fig. 2.—Another surface view of melanocytic striae in scar in Negro skin. Here the tensile forces were less uniform so that cross ridging is seen more frequently than in Figure 1; about × 20.

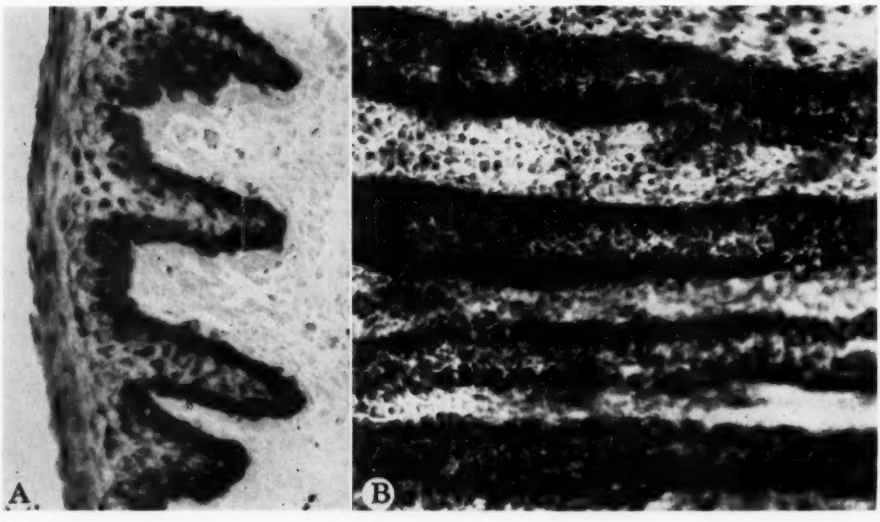
of pigment extending across the entire scar. Here and there throughout the scar and at the border, as the scar merges with normal skin, one can see an interruption of this linear pigmentation by small oval or circular pigmentary patterns. The latter are similar

Fig. 3.—Surface view of corium of scar after removal of epidermis. Here one sees the regular linear ridging and papillary formation which determines the pattern of epidermal growth and hence the melanocytic striae. Reduced about 15% from mag. × 28.

Fig. 4.—Surface view of corium of normal skin site after removal of epidermis. Contrast this large floral papillary surface of the normal corium with the fine linear ridges seen in the scar in Figure 3. Reduced about 15% from mag. of ×28; identical with that of Figure 3.

to what one sees in normal, noncicatricial skin. However, the ovals or circles are strikingly reduced in over-all dimension in the scars as compared with the normal skin. This difference, as well as all of the changes described above, are illustrated in the accompanying photographs (Figs. 1-6). The color cannot be obliterated by diascopy, nor

Fig. 5.—Views to show melanocytic nature of linear striae seen in scar of Figure 1. *A*, histologic cross section of scar stained with silver to show melanocytes and melanin capping in keratinocytes. This demonstrates what is being viewed in Figure 5*B*. Reduced about 20% from mag. ×360. *B*, surface view of epidermis of the scar, but now taken at a magnification about 20 times greater than Figure 1. By comparing *B* with *A*, it can be appreciated that the four dark striae do result from a depth view of melanocytes along the rete ridges of the epidermis. Further note that the dark striae may have a lighter central zone corresponding to the poorly visualized melanocytes at the bottom of the rete ridges of the epidermis. The light bands between the striae result from the relatively few melanocytes and little melanin overlying the dermal ridges.



do the position or shade of the striae vary as observed over long periods of time. We have observed them on several scars of more than 20 years' duration. Indeed, the change appears to be a permanent one. Finally, it is to be noted that the bands between the pigmented striae are light and relatively nonpigmented.

By removing the epidermis [1] from biopsy specimens, it was possible to demonstrate that the pigment was in the epidermis. Histologic study revealed it to be melanin, and gross observation of the surface of the underlying corium (Fig. 3) gave a ready explanation for the linearity of the pigment bands. The surface of the corium in the scar areas showed regular longitudinal ridging, in contrast to the papillary patterning seen in normal control skin specimens (Fig. 4). This is well illustrated also by Horstmann [2] in his recent superb monograph on the anatomy of the skin. This ridge patterning is determined by the lines of force and tension which are operative during healing (Langer's lines). This in turn governs the epidermal growth pattern, since regeneration here is an interplay of corium and epidermis. We can thus see that in the scar the epidermis grows long linear rete ridges down into the grooves in the corium. These ridges can be observed by direct inspection of the underside of the epidermis. In normal skin these epidermal rete ridges are not linear but are oval or circular in outline, always, however, corresponding to related oval or circular grooves in the corium (Fig. 6). The interposed corium between the epidermal rete ridges forms the dermal papillae. In scars, the dermal papillae are seen as the "white" lines between the melanocytic striae. They are correspondingly linear, since they are governed by the same physical forces and tension of the tissue which control the healing process.

Closer examination of the skin of the scars under higher magnification ($\times$ 30) revealed that the melanocytic striae which were visualized as dark solid lines grossly could be further broken down into three distinct linear components, a central, wider, more lightly pigmented zone flanked on each side by a narrower, more intensely pigmented line. This is well illustrated in Figure 5. These three zones within the melanocytic striae may be accounted for, since, upon looking from the skin surface down into the epidermis, one naturally sees a far greater number of melanocytes aggregated along the sides of the dermal ridges

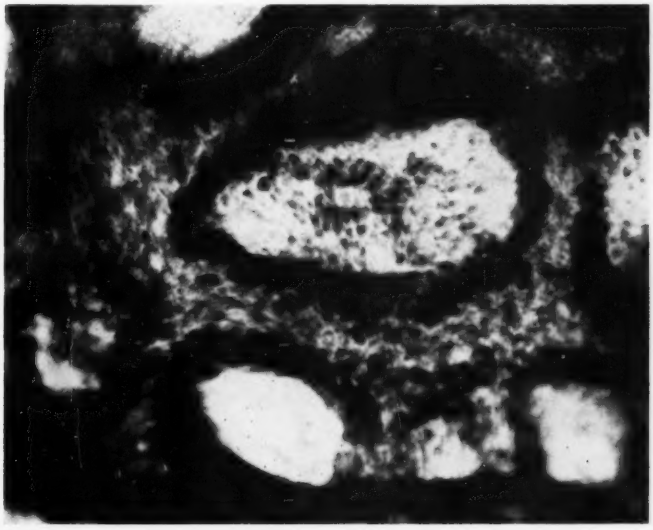


Fig. 6.—Surface view of pigment pattern of epidermis in normal skin. Here the oval light areas correspond to the dermal papillae, whereas the darker net reflects the epidermal downgrowths. Here again the intensely dark bands are over the melanocytes seen in depth along the sides of the epidermal downgrowth. The intermediate color is from melanin in the rete ridges of the epidermis. Contrast this normal papillary patterning with the linear one seen in scars. Reduced about 15% from mag. $\times$ 360.

than in the valleys. This optical effect resulting from viewing melanocytes "in depth" can best be appreciated by studying Figure 5 and by reference to the diagram of Staricco and Pinkus.[1] Under higher magnification the gross "white" lines of the scar between the melanocytic striae can be seen to be not entirely devoid of pigment cells. The melanocytic pattern of these "white" striae of scars is also illustrated in Figure 5.

Inasmuch as the linear ridging of the corium explains the melanocytic striae, one might expect to see this pigment banding in any areas in which linear ridging occurs. Normally one does find such linearity of growth processes at the distal extremities. The nail bed presents the most perfect example of this.[2] Although melanocytes are normally absent, the appearance of nevi in the nail matrix may produce gross clinical evidence of this linear ridging in the form of pigmented bands (Fig. 7). This has been described by a number of authors.[3]

Fig. 7 (Courtesy of Albert M. Kligman, M.D.). This white patient developed this dark band as a result of a junction nevus of the nail matrix, demonstrated by biopsy. The band is composed of numerous brown striae similar to those seen in scars. Here, in nail growth, the same linear forces are normally operative as in wound healing.

The pigmented striae of scars are a perfectly normal finding and provide insight into some of the basic mechanisms which are operative in wound healing. Although epidermal regeneration and indeed some attempt at dermal papilla formation is seen to occur in scars, cicatricial skin is not quite normal in this regard, and nature appears to have been thwarted by the physical or mechanical forces of the tissues surrounding the defect. It would seem that the melanocytic striae of scars described herein would serve as an excellent visual indicator for investigation of the fundamental changes concerned with wound healing.

Summary

Attention is drawn to the clinical finding of pigmented striae in human scars. Best visualized in Negro skin, these brown linear striae alternate with "white" striae. It has been shown that these brown striae represent the melanocytes along the epidermal ridges. In turn, the white striae reflect the reduced melanocyte population of the epidermis overlying the linear dermal ridges seen in scars.

Photographs by Edward F. Glifort Jr.

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Zirconium Granulomas of the Glabrous Skin Following Treatment of Rhus Dermatitis

Report of Two Cases

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Since the fall of 1956,[1] granulomas of the axillae following the use of a stick type deodorant containing sodium zirconium lactate have been reported in increasing numbers. Their location has been invariably confined to the axillae, and they appear as reddish-brown discrete papules, 1 to 4 mm. in diameter. Shelley and Hurley[2] have recently reviewed 64 cases previously reported and added 6 of their own. To date, there has been no evidence of skin reactions following the use of the insoluble hydrous zirconium oxide which has long been used in large quantities for treatment of Rhus dermatitis.[3]

The following report consists of two additional patients with zirconium granulomas, one of which occurred on the glabrous surfaces of both forearms and neck after repeated applications of hydrous zirconium oxide over an 18-month period.

Report of Cases

CASE 1.—A 50-year-old Caucasian woman was treated in March, 1956, for a Rhus dermatitis of the face, neck, and arms with a zirconium oxide lotion and oral steroids. Recurrence of the dermatitis in July, 1956, was again controlled with oral steroids and a tripelennamine-zirconium oxide cream topically. A papular eruption has remained on her anterior neck and forearms since that time. Subsequent pruritic, vesicular eruptions in these areas, assumed by the patient to be caused by poison oak, were treated by repeated applications of the zirconium oxide preparations. The patient had never used a stick type deodorant. Her general health and past history were otherwise unremarkable.

Physical examination at Letterman Army Hospital, Nov. 19, 1957, revealed numerous 1 to 4 mm. firm reddish-brown waxy papules distributed over the flexor surfaces of both forearms (Fig. 1) and the anterior neck region. The remainder of the examination was within normal limits.

Fig. 1 (Case 1).—Reddish-brown papules over the forearms after prolonged self-treatment with zirconium oxide medications. "U. S. Army Photograph."

Histopathologic examination of a papule from the left forearm on Dec. 2, 1957, showed aggregates of epithelioid cells and Langhans' giant cells in the upper dermis (Fig. 2). Special stains for acid-fast bacilli and fungi were negative. No foreign material could be detected with polarized light.

Laboratory studies, including a complete blood cell count, urinalysis, cardiolipin microflocculation test for syphilis, serum calcium, total serum proteins with albumin-globulin ratio and x-rays of the chest and hands were all within normal limits. Histoplasmin, coccidioidin, and PPD No. 1 and No. 2 skin tests were negative.

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Fig. 2 (Case 1).—Photomicrograph of Figure 1, showing typical granulomatous pattern with scattered giant cells. Hematoxylin and eosin; × 100. "U. S. Army Photograph."

Patch tests on Jan. 6, 1958, to 4% zirconium oxide lotion and ointment, full strength, showed no reaction in 48 and 72 hours. On Feb. 7, 1958, a 2×2 mm. area over the left lateral thigh was abraded by the standard vaccination multiple-pressure technique, following the application of a lotion containing 4% zirconium oxide. No visible blood was observed on the skin after this procedure. Biopsy specimen on March 31, 1958, of a brownish-red nodule over the previously abraded site showed nests of epithelioid cells in the upper corium. The same procedure was repeated on the right lateral thigh with use of a 1:100 dilution of the 4% zirconium oxide lotion with the appearance of a reddish-brown papule two weeks after the application (Fig. 3). Biopsy of this nodule at the end of four weeks revealed the same granulomatous reaction as that previously described (Fig. 4).

The eruption over the forearms and neck has gradually diminished over the 12-month period since her initial examination.

Case 2.—A 31-year-old Caucasian woman developed a pruritic inflammatory rash, confined to the axillae, in February, 1957, two months after using a commercial zirconium deodorant stick. Her pruritic symptoms were not relieved by various

Fig. 3 (Case 1).—Reddish brown nodule, right thigh, one month after testing with a 1:100 dilution of 4% zirconium oxide. "U. S. Army Photograph."

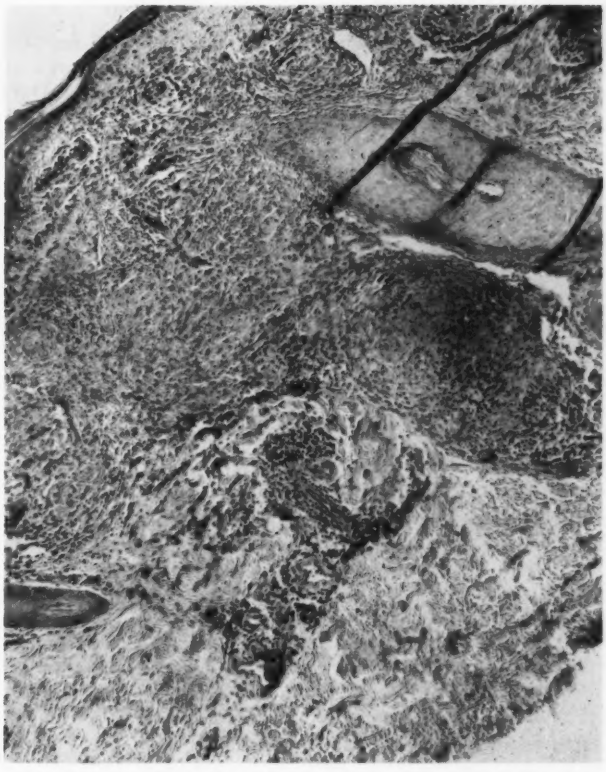

Fig. 4 (Case 1).—Photomicrograph of Figure 3, showing granulomatous infiltrate. Hematoxylin and eosin; × 100. "U. S. Army Photograph."

topical preparations, including 1% hydrocortisone ointment. Transient relief and moderate regression of the lesions was obtained in April, 1957, after a course of superficial x-ray, only to recur one month after the treatments were terminated.

Examination at Letterman Army Hospital, Aug. 20, 1958, revealed multiple reddish-brown papules limited to the axillae. Biopsy specimens showed a sarcoid-like granuloma confined to the upper corium. Patch tests to zirconium oxide lotion were negative in 48 and 72 hours. On Aug. 22, 1958, a 2×2 mm. area over the left lateral thigh was abraded by the multiple pressure technique following the application of a 1:100 dilution of 4% zirconium oxide lotion. A reddish-brown papule appeared after approximately two weeks and was biopsied at the end of four weeks. Histopathologic examination showed the typical granulomas.

No skin reactions were observed on 10 normal male subjects two weeks after the application by the multiple-pressure technique of both full strength and 1:100 dilution of 4% zirconium oxide lotion.

Comment

Zirconium compounds have long been known to have a low toxicity for animals and man.[4] Workers of one large industrial company have been handling zirconium for some 40 years with no recorded incidence of toxic reaction or inflammation. The insoluble zirconium oxide or carbonate has been used by thousands of patients in the treatment of Rhus dermatitis with no recorded reactions.[5-7] It is felt that the very low but definite sensitizing potential of zirconium, combined with minimal penetration of the insoluble zirconium oxide through the excoriated skin, can best explain the first patient's rare granulomatous response to this relatively inert substance. Prior et al.[8] produced acute inflammatory reactions and typical granulomatous lesions after the subcutaneous and intracutaneous injections of various solutions of sodium zirconium lactate and/or sodium stearates. Shelley and Hurley[2] demonstrated in man that the delayed granulomatous reaction is an allergic response to extremely small

amounts of the zirconium ion and not due to a particular salt or impurity of zirconium. In support of this concept, it is of interest that experimental granulomas were produced with a 1:100 dilution of 4% zirconium oxide in both of our patients, although one was sensitized initially by the topical application of a different salt of zirconium.

Summary

A case of zirconium granulomas of the glabrous surfaces of the forearms and neck due to topical applications of zirconium oxide is reported. An additional case of axillary granulomas due to sodium zirconium lactate is also reported. Experimental granulomas were produced in both of these subjects by using the multiple-pressure (vaccination) technique and a 1:100 dilution of 4% zirconium oxide. The mode of action is thought to be an allergic sensitization to the zirconium ion rather than to a specific salt of zirconium or impurity. No skin reactions were observed on 10 normal male subjects two weeks after the application by the multiple-pressure technique of both full strength and 1:100 dilution of 4% zirconium oxide.

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Argyrosis and Cyanosis—Melanosis and Cyanosis

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Silver enters the body in various chemical combinations, the most popular in the past being silver nitrate pills ingested over a period of years for gastrointestinal ailments. This form of therapy is no longer in use. Silver, however, still enters the body in the form of nasal drops or eye drops or as a result of handling the metal (silversmiths). Silver is not excreted like most drugs but remains in the body, deposited permanently in the skin, producing a gray-discolored skin.

The shade of gray may be very light or very deep according to the area of the body and the amount of silver stored in the cutaneous surface. Parts exposed to sunlight are deep gray. When the shade of gray is very deep, the diagnosis of argyrosis is obvious. Difficulty arises when the amount of silver taken in was small and the shade of gray is light. Difficulty also arises when the silver is deposited in certain areas in which other conditions may produce similar discoloration; for example, the nails may be blue or bluish and perhaps drumstick shaped in congenital heart disease. A patient with argyrosis, in coma, presents a peculiar shade of bluish-gray which may obscure the diagnosis of argyrosis (figure, top left).

Cases have been reported [1] in which families worried about their children kept in because of cyanosis allegedly due to congenital heart disease, whereas, the gray discoloration of the skin, mucous membranes, and nails was, in fact, argyrosis, due to the use of silver nose drops.

A 50-year-old man of Mediterranean extraction took silver nitrate nose drops for years. The addition of silver to his already naturally dark skin produced a mixed shade of olive-gray, not characteristic of argyria. The nails, however, were strikingly blue-gray (middle left). Each time he was examined by a new physician, a search was made to determine the type of cardiac disorder responsible for the discoloration of the nails and skin.

In investigating the etiology of bluish skin coloration, besides congenital heart disease, heart failure, argyrosis, and melanosis, the possibility of the handling of blue rinses (hairdressers) and of the handling of typewriter ribbons (stenographers) must be considered.

Edwards et al.[2] show excellent photographs of hands and nails before and after lobectomy for congenital pulmonary arteriovenous fistula; disappearance of cyanosis and clubbing is demonstrated.

Bearn and McKusick [3] show azure lunulae in two patients with hepatolenticular degeneration.

Figure upper left shows a combination of the gray of argyrosis with the cyanosis of heart failure.* A hand of a nurse was included to compare with normal skin color. The patient was hospitalized in coma and no relative was there to tell about the patient's past history. The ghastly bluish-gray discoloration was different from plain argyrosis and remained a puzzle for a while. Various chemical intoxications were suspected. Deep-gray color was found in the

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* It is interesting to note the cadaveric color in the paintings left by the masters. In practically all entombments, the skin of Christ is of the same color as the surrounding living figures. A striking exception to this apparent rule is the Deposition from the Cross by Rembrandt at the Ringling Museum in Sarasota, Fla. In this masterpiece the body of Christ is truly cadaveric and with a bluish shade, strikingly resembling the color of combined argyrosis and cyanosis.

spleen, in the kidney (upper right), in the cervical, and vaginal mucosa.

Another rare occurrence and a diagnostic problem is the rapid change from a white skin into a black one in generalized melanosis from internal melanoma. This is described as blue-gray or argyria-like in the three cases of this kind reported in the literature.[4-6]

A fourth instance is similarly rare. A change of a white skin to a Negro-like one within six months before death from Hodgkin's granuloma was reported by Piaggio Blanco, Montero, and Grosso.[8] Melanuria and melanin determination are discussed by Rothman.[9] Melanin and the endocrine system are also discussed by Deutsch and Mescon[10] and by Boutelier.[11] Cutaneous manifestations of internal malignant tumors are investigated by Becker et al.[12]

A peculiar darkening of the skin has been reported by Thiers et al.[13,14] in a few cases of chronic nephritis. A universal pigmentation described as bluish-black, darker than in argyria, suggestive of an advanced case of acanthosis nigricans, due to ingestion of phenolphthalein in laxatives over a period of years is reported by Weiss and Kile.[15] Lutenbacher[16] discusses hyperpigmentation in certain cardiac disorders. Generalized melanoderma from internal melanoma is nicely illustrated in color by Albeaux-Fernet et al.[17] The shade of the pigmentation varied from brown-black, with "reflects métalliques" on the face, to pencil-like lead on the thorax, to bluish-gray on the abdomen. They mention ten previous observations, presumably, of the same kind. Melanosis in melanosarcoma is reported by Møller.[18] Diffuse deep-gray pigmentation is reported by Linquette et al.[19] in a 55-year-old woman with acute leukemia, a few days after one injection of 500 mg. of 17-alpha-hydroxycorticosterone.

Figures middle right and lower left are of an elderly white man with a decidedly white skin up to three months before death. The color was really bluish-black and resembled a combination of argyrosis and cyanosis. The man was comatose, and no relative was present to tell about his past history. The color of the nails (lower left) was also bluish-black. The urine did not become dark after emission. It was voided coffee-black (lower right).

At autopsy, all the organs were black. Melanoma was found involving the liver, spleen, myocardium, lungs, kidneys, and lymph nodes. The urine was voided coffee-black because of the enormous amount of melanin present. The skin color was, therefore, due chiefly to a combination of increased melanin and probably superimposed cyanosis.

Summary

The color of the skin can furnish important information concerning internal disorders. One case of a combination of argyrosis and cyanosis of coma and one of generalized melanosis from internal malignant melanoma are discussed.

170 Waterman St.

Addendum

Color description and definition are important in medicine in general, and essentially in dermatology. To find the right term for that shade of red, blue, or yellow you wish to convey to the reader or discuss in class is often a task. Comparison with surrounding common colored objects is one way to convey the shade of color to the

Top left.—The combination of argyrosis and cyanosis of coma.

Top right.—Deposits of silver in the kidneys in argyrosis.

Middle left.—Bluish discoloration of nails in argyrosis in comparison with a normal nail (left).

Middle right.—Generalized bluish-black discoloration developed in three months in a white man with internal melanoma. The bluish-black shade is due to the combination of melanosis and cyanosis of coma.

Lower left.—Fingers and nails of the man of middle right figure.

Lower right.—Urine of man of middle right figure voided coffee black.

A-47-134

reader's mind. Appel (Decadent Descriptions in Dermatology, *Arch. Dermat. & Syph.* 62:370-379 [Sept.] 1950), had good reasons to object to this type of comparison. To compare the appearance of a nodule of lupus vulgaris under glass pressure to the color of apple jelly is faulty because a student may not be familiar with apple jelly. The same applies for example to salmon-red, flesh color, etc.

A color chart universally adopted would be ideal. Appel suggested the use of the Munsell Book of Color of the textile industry. This book is good for the purpose it was made. Besides its cost, its use at the bedside or in the office is impractical. In a U. S. Government publication (The ISCC-NBS method of designing colors and a dictionary of color names, National Bureau of Standards Circular 553, Nov. 1, 1955, p. 158), besides the Munsell Book of Color of the textile industry, there are 14 other methods or systems of color designation, all for industrial purposes. In these one can find 138 different kinds of vivid red, 93 of strong red, 49 of deep red, 5 of very deep red, 161 of moderate red, 105 of dark red, 15 of very dark red, 37 of light grayish-red, 130 of grayish-red, etc. These descriptions are good for industrial purposes but certainly not for dermatology.

More practical would be, for instance, the use of colors and terminology of flowers or stamps. Here, again, certain flowers well known to a United States dermatologist would be perhaps unknown to a Chinese, and for the stamps, the hobby is not yet universal. Besides, a dermatosis is not made of one color, but of many right on the same spot. A skin manifestation may be made up of a palette of colors. One evidently cannot describe it as if it were the color on a house, a fabric, or a painting.

The least impracticable among the commercial charts is the Philatelic Color Guide, consisting of 101 colors. About 50 colors could be retained and made into a standard dermatologic color guide. Until such a chart is developed and agreed upon one has to go along with the time-honored orange-red, lobster-red, cardinal-red, salmon-red, heliotrope-violet, turquoise-blue, apple-green, olive-green, slate-gray, to convey the color attempted definition to the reader.

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An Epidemic of Infectious Erythema in Germany

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By the end of October, 1958, there occurred in Berlin an outbreak of an apparently new skin eruption which soon exploded into epidemic proportions. Similar cases had previously been reported from Kiel, Hamburg, Münster, Bremen, and Osnabrück, which caused the disorder to be named morbus Osnabrück (*Osnabrücker Krankheit*). The high incidence of the rash caused considerable concern among the public, which was increased by alarming articles in the tabloids warning against a mysterious new skin disease. Thus, the common and traditional, almost mystic, fear of skin infections caused school classes to be closed and workers to be sent home from their jobs, and it even overshadowed the political uneasiness in the former capital.

Gradually, a more sober evaluation of the spreading disorder took place, and it became evident that this was not a "new" skin condition but that it was identical with the erythema infectiosum, also known as "fifth disease." The first description had been given as early as 1886, by Anton Tschamer, in Graz, who had considered it as a special type of rubeolae. To Sticker, in Giessen (1899), goes credit for having recognized the rash as an entity and given it the appropriate name. Six years later Shaw called the attention of American medicine to this exanthem, which he had observed during a visit to Vienna. In the following decades numerous reports on isolated endemics were published in Europe (France, Italy), Asia (Turkey), and in the United States.[1] It is curious to note that in 1956 physicians in Hawaii, unfamiliar with the eruption, called it "infectious blushing," a name befitting the romantic environment of the victims.

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From the Skin Clinic of the Free University of Berlin (Director, Prof. Dr. Spier).

The recent outbreak in Germany and, particularly, in Berlin, presented certain interesting features and deviations from the hitherto-described clinical picture that will be recorded in the following report.

This is based on our experiences in over 200 cases treated within a month's period at the skin clinic of the Free University and in a busy panel practice in a densely populated borough of Berlin (Neukoelln, American Sector). There were more than twice as many women affected as men; adolescents and middle aged people were more affected; the oldest patient seen was an 81-year-old man. Children among those affected were decidedly in the minority, an observation confirmed through inquiries; however, we gained information that dozens of cases were noted in different kindergartens throughout the city, and in school classes the incidence ranged from isolated cases to a morbidity of some 20%.

As concluded from family transmissions, the incubation period seemed to fluctuate from five or six days to two weeks. As a rule, the exanthem appeared overnight, without premonitory symptoms; occasionally, patients volunteered that they had noticed signs of a head cold or sore throat prior to the onset. There was no fever, sometimes elevated temperature, no enlargement of the lymph nodes, and no malaise, as far as the milder cases were concerned. These resembled measles and rubeolae, presenting a rosy-red maculopapular eruption, beginning on hands and arms, also in the face, and rapidly spreading to trunks and lower extremities, including the soles. As more and more people became affected, the rash assumed a rather bizarre and polymorphous appearance. Even in the same person it varied from a morbilliform distribution

on face and limbs to huge coalescent patches of a bright red hue, covering the greater part of the body surface, sometimes changing to hemorrhagic lesions, especially on the legs. There was frequently swelling of the face and, in women, edema of the arms, resulting in tightness of the skin. In other cases, urticaria and erythema multiforme-like changes were prevalent. Rarely, formation of vesicles, sometimes grouped in herpes simplex-like fashion, was noted. In severe cases which had to be hospitalized, general symptoms, such as fever, rheumatic pains, prostration, and circulatory disturbances, were more or less pronounced. It must be stated that the severity was not dependent on the age group. In mild and abortive cases, subjective symptoms were limited to itching, moderate to severe, particularly on the soles and in the gluteal region; sometimes patients complained of a burning sensation.

On careful examination, the mucous membranes were found to be involved in the majority of cases, chiefly in form of sharply outlined dark-red spots on the gums, soft palate, uvula, and pharynx, associated with some soreness. Occasionally, vesicles of different size were noted, even small ulcers. Similar lesions could be demonstrated in the genital zone: balanitis and vaginitis with pruritus and discharge. In a few instances the conjunctivae were also inflamed.

The blood status was not characteristic. In fresh cases there was an increase of the white blood cells, with a shift to the left and toxic granulations; later, monocytosis and often marked eosinophilia (up to 34%) were noted.

The histopathology studied by one of us (H. G.) in 10 cases was that expected in an acute erythema, showing the signs of an exudative process. There was edema, dilation of the blood vessels, with perivascular infiltration consisting of lymphocytes with occasional plasma cells. Vesicles and hemorrhagic lesions presented the customary pictures.

As in previously known outbreaks, the infection was always self-limited and cleared after lasting from 4 to 20 days, sometimes terminating with more or less marked desquamation and a mottled appearance of the skin (due to vasomotor disturbance), leading to slight pigmentation. Sometimes the seemingly faded rash was rekindled by a hot bath or similar stimulation of the skin. However, we encountered a few cases where a genuine recidive occurred after a free interval of 8 to 10 days.

The treatment was, of course, symptomatic, consisting in high fluid intake, large doses of ascorbic acid (the standard German diet does not include the luxury of citrus fruits), calcium, and antihistaminics, as well as application of antipruritic lotions. In severe and generalized cases, hospital care with administration of corticosteroids was required, facilitated by the fact that hospitals in Berlin have a relatively large number of beds for dermatological and infectious diseases.

This outbreak, which abated after a period of less than four weeks, is of particular epidemiological interest. In the first place, in contrast to previously observed endemics in orphan asylums, children's hospitals, and similar institutions, this was a true epidemic with a morbidity estimated at about 50,000 cases in Berlin (there had been an epidemic in the Loire Valley in 1950-1951, affecting over 1,000 people). While formerly mainly children were attacked, this time adults, particularly women, were in the majority. This might point to a possible transmission of the agent through foodstuffs, as these are mostly handled by women, although some authors believe in transmission by direct close contact. At any rate, contagiosity is apparently slight; mutual infection of family members occurred in less than 10%. It seems that the disorder originated in the northern part of the German Federal Republic and spread in a southerly direction, following the highways. The infectious agent is obviously a virus, such as demonstrated by Werner, closely resembling

that of measles; this has been confirmed by its cytotoxic effect as well as by titration and complement-fixation tests. The differences from the hitherto described symptomatology, especially the frequent severity of the lesions, can be explained on the basis of a mutation of the virus (as known in other virus diseases), either resulting in increased virulence of the agent or in breaking through the barrier of specific immunity against the "common" type of virus.

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Chromoblastomycosis Treated by Vibrapuncture Injection of Amphotericin B

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Chromoblastomycosis, although not one of the fatal fungus diseases, is sufficiently disfiguring to demand treatment. In the past year, we have had success in treating a case of this disease with amphotericin B, with use of the vibrapuncture technique.

Report of a Case

A 74-year-old Negro farmer presented himself to the Tulane Dermatology Service on March 18, 1958, with a granulomatous lesion of the left wrist, present for 11 months. It was ellipsoidal in shape; the semimajor axis was 5 cm. in length; the semiminor axis was 2.5 cm., and the area thus was approximately 39.3 sq. cm. There was central clearing. The borders were verrucous in some places and scaly in others. The lesion was infiltrative throughout much of its extent.

Scraping of the lesion disclosed the characteristic septate bodies of chromoblastomycosis. The fungus culture was identified as Hormodendrum pedrosoi. The biopsy specimen was read by Dr. Wallace H. Clark, of the Tulane Department of Pathology, as follows: Extensive hyperkeratosis, parakeratosis and marked irregular acanthosis, with extensive acute and chronic inflammation of the corium. One focal epithelioid reaction is noted, as well as many foreign-body giant cells. Fungus forms were seen in the dermis.

Initially, the lesion was infiltrated with amphotericin B, but after the report of Aaron, Kantor, and Stromeyer on the use of the vibrapuncture technique in the treatment of localized neurodermatitis, it was decided to use this method instead. Accordingly, 1 to 2 cc. of solution of amphotericin B made by adding 100 mg. to 10 cc. of water was placed on the lesion and tattooed through. This was repeated three times weekly over a three-month period. Improvement was seen almost immediately, and at the end of the treatment period there was complete regression. Moreover, the lesion was sterile by repeated cultures and the biopsy specimen was read as follows: Extensive dermal fibrosis with chronic inflammation. No organized areas of granulomatous inflammation similar to those seen in the first biopsy specimen are present.

Comment

Amphotericin B was isolated by Gold, Stout, Pagano, and Donovick from streptomycete Culture M 4575 derived from soil from the Orinoco river of Venezuela. It was shown by these workers to have a wide range of antifungal activity in vitro, and numerous clinical papers have verified the hope that these agents would be useful in the treatment of fungus disease. Cases of chromoblastomycosis have also been treated with amphotericin by Costello and DeFeo.[3] Favorable results have now been reported in the treatment of coccidioidomycosis,[7] cryptococcosis,[2] histoplasmosis,[5] and North American blastomycosis.[4]

The vibrapuncture technique seems to be a superior method of placing the antibiotic in contiguity with the fungus because it is easy, quick, and relatively painless as compared to local infiltration. The depth of the organisms can be determined by biopsy and the needle length adjusted accordingly. Moreover, the lack of side-reactions experienced by our patient will probably continue to be seen in other persons so treated in contrast to precardial distress and fever sometimes experienced when amphotericin B is given intravenously.

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From the Division of Dermatology, Department of Medicine, and from the Department of Microbiology, Tulane University School of Medicine.

Amphotericin B was furnished by Dr. John Groel, Associate Medical Director, The Squibb Institute for Medical Research. This material has the trade name of Fungizone.

Fig. 1.—Forearm of patient prior to treatment.

Fig. 2.—Response to three months of amphotericin B.

Summary

Amphotericin B introduced by vibra-puncture technique resulted in a cure of a case of chromoblastomycosis.

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The Effect of X-Rays, Grenz Rays, Thorium-X, and Radioactive Phosphorus on Superficial Mycotic Agents

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The results of a number of investigations of the effects of ionizing radiation on fungi have been contradictory. Pearson et al.[1] found that 1,100 r of high-voltage x-ray or exposure for 24 hours to 20μc. of radioactive iodine or radioactive phosphorus caused partial to complete inhibition of growth of a number of fungi, such as Epidermophyton floccosum, Microsporum audouini, Microsporum gypseum, Trichophyton rubrum, and Trichophyton violaceum.

Lewis et al.[2] exposed M. gypseum and Trichophyton mentagrophytes to 4,800 r of x-ray either in a single dose or in repeated doses and found a speeding up of maturation as evidenced by a more rapid development of the core of the fungus culture. Comparable doses of soft radiation showed no such enhancing effect.

Lawrence et al.,[3] using Co^{60} as a source of radiation, found that, for the production of sterility, Aspergillus niger required a dosage of 340,000 rep and Penicillium notatum 255,000 rep. Saccharomyces cerevisiae was inactivated 99.99% by 70,000 to 340,000 rep. Similar doses of x-ray had the same effect on this yeast. Bacteria such as Proteus vulgaris and Escherichia coli required 289,000 rep for sterilization, whereas with Bacillus subtilis, 2,040,000 rep were needed.

In view of these contradictory reports, it seemed to us to be of some interest to review this problem and to determine the effect of a variety of dosages of different types of radiation on superficial mycotic agents.

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From the Division of Dermatology, Department of Medicine, University of Miami School of Medicine.

This study was supported in part by U. S. Army Contract No. DA-49-007-MD-731 and by a research grant from the Public Health Service (E-1546).

Materials and Methods

The following organisms were used in our study: M. audouini, M. canis, T. concentricum, E. floccosum, T. gallinae, M. gypseum, T. megnini, T. rubrum, T. schoenleini, T. tonsurans, and T. verrucosum. In addition, Candida albicans was employed in a few experiments.

Cultures of the above organisms were grown in Sabouraud's dextrose broth containing 0.5% yeast extract and shaken in 50 ml. flasks on a Gyrotory shaker. Cultures were one week old when used. This method results in the formation of fungal pellets. Small pellets of uniform size, approximately 1 to 2 mm. in diameter, were selected. For the experiments with 390,000 r and 600,000 r of Grenz rays, these pellets were broken into smaller pieces in a blender. The same strain of each organism was used throughout all the experiments, fresh transfers being made at regular intervals.

In the experiments with radioactive isotopes, concentrations of 300μc., 150μc., and 75μc. per ml. of thorium X and 1,000μc., 500μc., 300μc., 250μc., 150μc., and 75μc. per ml. of P^{32} were prepared. One milliliter of the appropriate concentration was placed in a well of a porcelain plate. The pellet of organism was added to the liquid and stirred thoroughly with a platinum wire to obtain maximal wetting with the isotope; the mixture was allowed to stand for 24 hours. The pellet was then rinsed twice in isotonic saline and transferred either to a Sabouraud slant or a Sabouraud plate and observed at 24-hour intervals for two weeks. Controls were run with all organisms, using normal saline instead of isotope. The thorium X solution, being somewhat acid, was adjusted to pH 7 by the addition of anhydrous sodium carbonate.

Thorium X contains about 4% of calcium chloride, necessitating controls with this concentration.

In the experiments with x-ray and Grenz ray, the pellets were placed on Sabouraud's medium in Petri dishes and treated with the doses indicated. The dish cover was removed during the exposure. The x-rays were delivered by a machine with the following constants: 250 kv., 30 ma., 13 cm. dis-

TABLE 1.—*Results of Treatment of Fungi with Various Radiations* *

Fungus	Abbreviations Used in Photos	Dosage, μc/Ml. * Thorium X 300	Thorium X 150	Thorium X 75	Radioactive Phosphorus 1,000	Radioactive Phosphorus 500	Radioactive Phosphorus 300	Radioactive Phosphorus 250	Radioactive Phosphorus 150	Radioactive Phosphorus 75
M. audouini	Au	—	++	+++	+	++	++	++	++	+++
M. canis	Ca	+	0	0	—	++	++	++	++	+++
T. concentricum	Co	+	++	+++	—	++	++	++	++	++
E. floccosum	Fl	+	+++	+++	+	++	++	+	+++	+++
M. gallinae	Ga	+	++	++	+	++	++	+++	++	+++
M. gypseum	Gy	+	+	+	+	+	++	++	++	++
T. mentagrophytes	Men	++	0	0	0	0	+++	0	+++	+++
T. megnini	Meg	—	+	++	++	++	++	++	+++	+++
T. rubrum	Ru	—	+	++	0	+	++	++	++	++
T. schoenleini	Sch	+	0	0	+	—	++	++	+++	+++
T. tonsurans	To	+	++	++	—	+	+	+	+	+
T. verrucosum	Ve	—	+	++	—	+	+	+	++	++

* — indicates no growth; + slight growth; ++, moderate growth; +++, good growth; 0, no data obtained.

tance, no filtration, half-layer value 2.0 mm. Al, giving a dose of 5,325 r per minute. Grenz ray dosage per minute was 10,000 r, produced by a machine with 15 kv., 9 ma., at a distance of 4 cm.

A C. albicans suspension was prepared in Sabouraud's dextrose broth with 0.5% yeast extract and left for 24 hours on a Gyrotory shaker. A dilute saline suspension of the yeast was poured over the entire surface of a Sabouraud plate. The cover was removed and replaced by a sheet of lead with a central opening 3 cm. in diameter during the time of treatment with Grenz rays. The organisms were then exposed to 90,000 r and 190,000 r of Grenz rays.

Results

The results with fungi are summarized in Tables 1 and 2. All types of radiation employed produced partial or complete inhibition of growth.

Thorium X in a dosage of 300μc. per milliliter applied for 24 hours was more effective than the same dosage of P^{32}. Thorium X in this dosage produced complete inhibition of M. audouini, T. megnini, T. rubrum, and T. verrucosum, whereas the same dosage of P^{32} did not produce complete inhibition of any fungus. It required more than three times this dosage, or 1,000μc. of P^{32} per milliliter to produce complete inhibition of M. canis, T. concentricum, T. tonsurans, and T. verrucosum.

Controls with 4% calcium chloride solution permitted normal growth.

TABLE 2.—*Results of Treatment of Fungi with Various Radiations*

Fungus	Dosage, r X-Ray 300,000	X-Ray 200,000	X-Ray 100,000	X-Ray 20,000	Grenz Ray 600,000	Grenz Ray 390,000	Grenz Ray 285,000	Grenz Ray 165,000
M. audouini	—	—	++	0	0	+	++	+++
M. canis	—	++	+++	0	—	+	+++	+++
T. concentricum	0	0	+	0	0	0	+	0
E. floccosum	0	0	+	++	0	0	+	0
M. gallinae	—	—	++	0	0	+	++	+++
M. gypseum	—	—	+++	0	—	—	+++	+++
T. mentagrophytes	—	—	+++	0	—	—	—	++
T. megnini	0	0	++	+++	0	0	+	0
T. rubrum	+*	—	++	++	0	—	+	++
T. schoenleini	—	—	++	+++	0	—	+	++
T. tonsurans	—	—	++	++	0	—	+	++
T. verrucosum			+	+	0	0	—	0

* Culture after 2 wk. 1 mm. in diameter compared to 15 mm. for control.

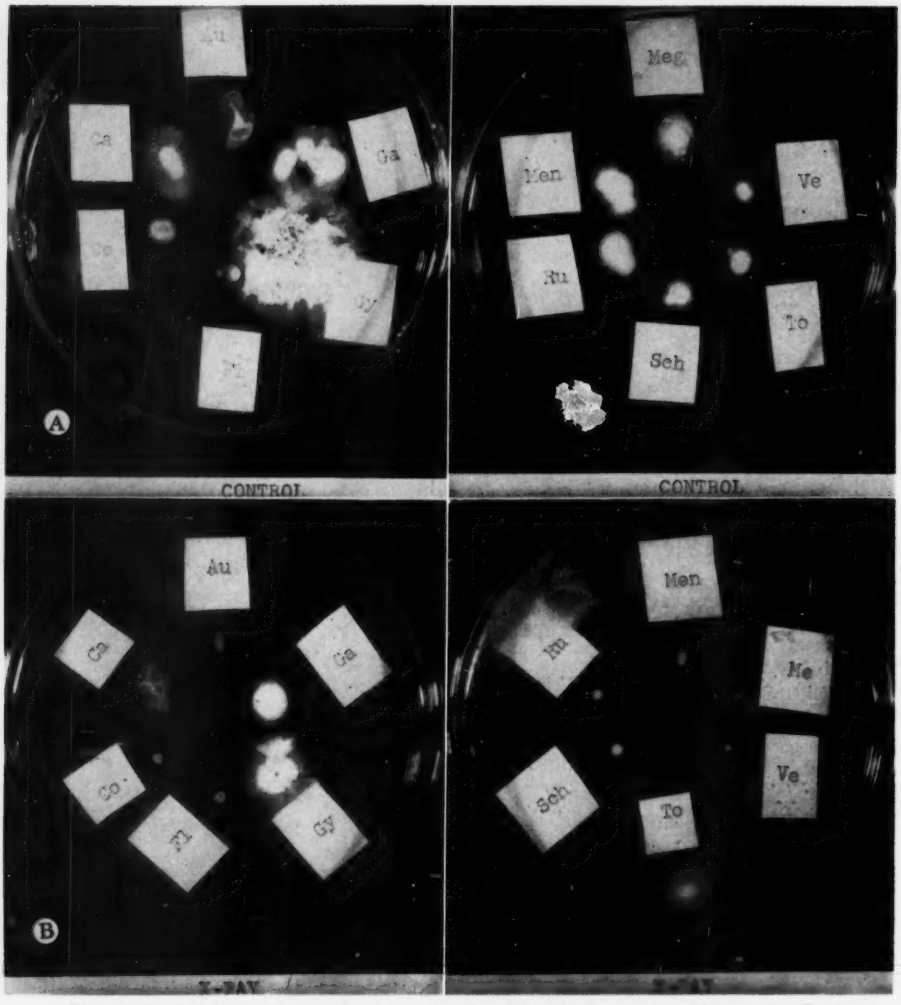

Fig. 1.—*A*, the upper photographs show controls of fungi after one week's growth. *B*, the lower photographs show similar fungi one week after treatment with 100,000 r units of x-ray.

A dose of 100,000 r units of x-ray permitted growth of all fungi but at a markedly inhibited rate; 200,000 r units resulted in complete inhibition of all the fungi tested with the exception of M. canis, which, however, yielded to 300,000 r units (Figs. 1 and 2).

Grenz rays also inhibited the growth of fungi. The dosages required to produce complete inhibition were somewhat larger than those required with deep x-ray. It is possible that some of the masses of fungi were not completely penetrated by the Grenz rays, resulting in the need for higher doses.

With C. albicans, a thin suspension was spread over Sabouraud's agar, thus permitting the soft Grenz rays to penetrate the mass completely. The center of the suspension was treated and the outer half covered by lead served as control. With 95,000 r the central area remained clear for three

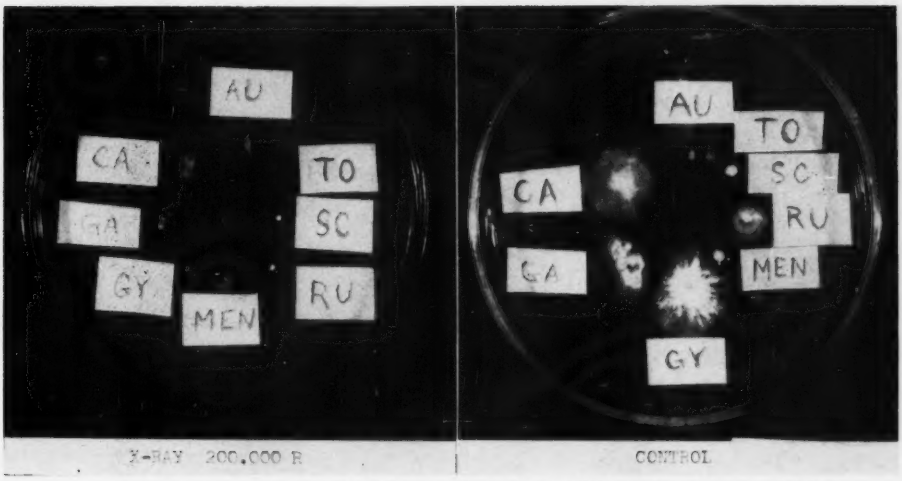

Fig. 2.—Similar experiments as in Figure 1, but with 200,000 r units of x-ray. Inhibition is almost complete.

days, whereas the peripheral area was covered with colonies too numerous to count. On the fourth day, discrete colonies about 1 mm. in diameter began to form in the center (Fig. 3).

With 190,000 r of Grenz ray, there was complete inhibition of the C. albicans with no growth in the center after two weeks (Fig. 4).

Fig. 3.—C. albicans exposed to 95,000 r units of Grenz ray. Photograph four days after exposure, showing beginning of colonies in treated area.

Fig. 4.—C. albicans exposed to 190,000 r units of Grenz ray, showing complete inhibition.

Microscopic Changes

The fungal pellets employed in this study constitute a relatively large mass of vegetative mycelia. For this reason, hyphal cells in which a mutation might occur are greatly outnumbered by normal cells; hence, mutations have slight opportunity to become manifest. In general, doses of radiation below the inhibitory level did not evidence mutagenic effects, as demonstrated by the colonies developing from the treated pellet. In a number of cases the subinhibitory doses appeared to produce a stimulatory effect, as shown by an acceleration of growth and the production of an increased number of conidial structures. The colonies developing from pellets exposed to a near lethal dose were generally characterized by a loss or reduction in the numbers of defined morphologic entities and occasional bizarre forms were observed. Most commonly this phenomenon was evidenced only in the early growth phases and normal colonies with typical morphologic structures reappearing with the passage of time. In a limited number of cases, developing colonies from pellets exposed to near-inhibitory levels produced sectors characterized by distinctive variations in pigment production and in the macroscopic nature of the mycelium. The commonest observation was a suppression of aerial mycelium to produce initial zones of glabrous or waxy growth. In all cases with subsequent growth these colonial variants, presumed to be genetic in origin, were overgrown or crowded out by contiguous areas of more rapidly growing normal mycelium.

Summary

All forms of ionizing radiation tested, namely α-rays of thorium X, β-rays of P^{32}, as well as x-rays of different wave lengths, produced inhibition in growth of several pathogenic fungi. In some strains subinhibitory doses appeared to produce a stimulatory effect as shown by an acceleration of growth and the production of an increased

number of conidial structures. Colonies exposed to a near-lethal dose were generally characterized by a loss or reduction in the numbers of defined morphologic entities. In some cases variations in pigment production and mycelium formation were observed.

Complete inhibition of fungi with x-ray required from 200,000 to 300,000 r units and with Grenz rays, 390,000 to 600,000 r units. With C. albicans, 190,000 r units of Grenz rays produced complete inhibition.

Dr. Harold E. Davis and Dr. Raymond Parks treated the fungi with the higher dosages of x-ray. The technical assistance of Carolyn C. Boyd and Carole Kaiser Leigh is acknowledged.

The Fleischman, Burd Co., New York, provided the supplies of thorium X.

Jackson Memorial Hospital (36).

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The Treatment of Emergencies

Those Which Occur in the Office Practice of Dermatology

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Emergencies occur so infrequently in office medical practice that the physician may find himself unprepared in differential diagnosis and appropriate treatment.

This is a review, presented *first* in very brief summary to furnish an instantaneous reference; followed by a more detailed discussion of the various types of reactions and their treatment and, finally, a resume of prophylactic methods, purposely placed in this sequence in the belief that that is the order in which anyone encountering an emergency will find more useful.

An abbreviated guide for extreme emergency is as follows:

Important points: supine posture, patent airway, proximal tourniquet, constant attendance.

	Drug	Dose, Ml.	Route
Anaphylaxis (protein)	Epinephrine	0.4	S. C.
	Corticosteroid		I. V.
Allergy (drug)	Epinephrine	0.2	S. C.
	Corticosteroid		I. V.
Local anesthetic (toxic absorption)	Pentobarbital	2	I. V.
Epileptic seizure	Pentobarbital	2	I. V.

In all cases of emergency place the patient in supine posture with constant attendance; cease or block administration or absorption of medicament if possible; and maintain a patent airway.

Epinephrine (1:1,000) solution, a barbiturate solution, an intravenous corticosteroid solution, and a syringe with needle should be available in every treatment room at all times.

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Diagnosis and Treatment of Emergencies

Anaphylactoid Reaction.—Anaphylactoid reactions usually occur after injection of medicaments incorporating a protein, such as antibiotics, liver extracts, pollens, vaccines, horse serum, or hormones. A total of 2,995 antibiotic reactions have recently been reported.[1] Of these, 1,070 were life-threatening and 809 were anaphylactoid reactions. The reported incidence of death[2] with these reactions is 9%.

Signs: These may include vomiting, colonic spasm with diarrhea, abrupt fall in blood pressure, subnormal temperature, pallor, cyanosis, thready pulse, and loss of consciousness.

Therapy: Apply a tourniquet and administer epinephrine (1:1,000) S. C., 0.2 to 0.5 ml., and repeat as indicated. Intravenous corticosteroid may be invaluable. Ether anesthesia can be useful to control spasms.

The tourniquet is applied proximal to the site of injection to delay absorption. For this reason it is wise where feasible to give such injections sufficiently distal on an extremity to permit a proximal tourniquet application. A sphygmomanometer makes the best tourniquet because it permits one to follow the blood pressure at the same time giving an index for the repetition and dosage of epinephrine. Intravenous injections of epinephrine in the uninvolved extremity may become necessary.

Allergy.—Allergic reactions can develop following injections of a local anesthetic medicament, antibiotic, pollen, or toxoid.

Signs: These may be bronchospasm, urticaria, and angioneurotic edema.

Therapy: Apply a tourniquet and give epinephrine (1:1,000) S. C., 0.2 to 0.3 ml., and follow as with treatment of the anaphylactoid reaction. Antihistaminics have been recommended, but variation of response might make them less valuable than reliable epinephrine for emergency use. Alarming responses, such as laryngeal edema or severe bronchiospasm, are rare, but in such cases intravenous corticosteroid, and, with laryngeal edema, a tracheotomy must be considered.

Local Anesthetic Toxic Absorption Reaction.—The absorption of a local anesthetic may be so rapid as to exceed the rate at which it is destroyed. Generally, this possibility is eliminated by the use of a total amount considerably below the possible toxic absorption rate level. However, accidental intravenous administration can suddenly precipitate this reaction.

Signs: These are biphasic for the autonomic, cardiovascular, and respiratory systems. The early reaction is characterized by excitement, pallor, rising blood pressure with bradycardia, hyperpnea, polypnea, nausea, vomiting, tremors, and convulsions. This early reaction may dominate the entire episode or with larger doses may give way to the second stage of the reaction in a few seconds.

The second phase is characterized by falling blood pressure, tachycardia, respiratory depression, unconsciousness, coma, and death.

Therapy: Treat immediately whether the reaction is definite or doubtful. Give intravenous injection with 5% pentobarbital (Nembutal) sodium solution. If the reaction is doubtful, give 1 ml. and hold the needle in place to watch progress. If the infiltration was local and into an extremity, apply a tourniquet proximally. If in the second phase marked apnea develops, the respiratory exchange must be maintained either by mouth-to-mouth breathing with patient, use of a Safar airway, a Kreiselman hand resuscitator, or artificial respiration, (It has been recently shown that artificial respiration is not nearly as efficient as mouth-to-mouth breathing.) Follow with treatment for shock if indicated.

Epileptic Seizure.—Epileptic seizures may occur without apparent provocation. In some of the cases the attack may be preceded by warning symptoms known as aurae and occasionally by a sinister outcry.

Signs: These are rapidly progressive or begin with sudden loss of consciousness and intense pallor of the face and blanching of the hands. This is usually promptly followed by general muscular rigidity of the decerebrate type, whereupon respiration usually ceases, and the skin is observed to resume normal color at first and then to progress to cyanosis. At this phase the tongue is often bitten. The pulse is thready and arrhythmic. However, in the great majority of cases the episode consists of no more than psychomotor seizure consisting of involuntary and meaningless acts which are transient and require no treatment.

Therapy: Therapy is primarily that of preventing injuries. Let the patient remain where he falls; remove adjacent objects that he might strike in the clonic stage, and insert gauze or a lead pencil between the teeth. Later, when stupor develops no attempt should be made to abbreviate this phase of repair and recovery. Pentobarbital, sodium, 5% solution, may be injected intravenously. Start with 2 ml. in adults (see "Pentobarbital" below). In most cases the clonic phase is complete in 30 to 60 seconds and medication interference is unwarranted.

Syncope.—Syncope, or fainting, is of importance because it must be promptly distinguished from other causes of unconsciousness. It is probably the commonest emergency occurring in the dermatologist's office. In a highly susceptible person it can be precipitated by the slightest provocation. The mechanism appears to be peripheral vasomotor loss of tone leading to visceral blood pooling and inadequate return to the heart. The resulting cerebral anoxia causes the loss of consciousness.

Signs: These are unconsciousness, pallor, and perspiration.

Therapy: This consists of using the supine position, with loosened collar. Reflex stimulation usually produces prompt recovery. The simplest and handiest stimulus is smelling salts. Others are a cold wet towel on the patient's face, slapping, or dilation of the anal sphincter.

Hemorrhage.—Hemorrhage from any cause is best controlled by *direct pressure* at the site of bleeding followed by tourniquet and ligation with absorbable (gut) surgical suture as warranted. Profuse arteriolar hemorrhage after wide abrasion of the face may occasionally require gauze packs of 1:1,000 aqueous epinephrine applied with pressure.

Excessive Dose.—Overdosage of *epinephrine hydrochloride* may occur with the use of local anesthetics containing epinephrine, or in the treatment of an impending anaphylactoid or allergic reaction.

Signs: These can be alarming. Beyond the frequent anxiety and tenseness can be seen a sharp rise in blood pressure, tremor, weakness, respiratory difficulty, and palpitation. Cerebral hemorrhage, angina pectoris, and ventricular fibrillation can eventuate. When possible, use a tourniquet proximally to the site of injection with periodic release.

Therapy: There is no antidote. Fortunately, epinephrine is rapidly destroyed in the blood stream.

Excessive doses of meperidine, alphaprodine, or pentobarbital should be counteracted with the correct antidote:

Drug	Antidote	Dose, Mg.	Route
Meperidine (Demerol) hydrochloride	Nalorphine (Nalline) hydrochloride	5-40	I. V.
Alphaprodine (Nisentil) hydrochloride	Nalorphine	5-40	I. V.
Pentobarbital sodium	Picrotoxin	1-10	I. V. or I. M.

Sclerosing Agents.—Sclerosing agents such as invert sugars and 20% sodium chloride are relatively safe except for possible slough and vascular cramps. With sodium psylliate (Sylnasol) renal colic has been reported. Sodium morrhuate (sodium soap of the fatty acids of cod liver oil) and Monoethanolamine oleate (an ester of a fatty acid) are capable of producing an anaphylactoid reaction (use 0.2 to 0.5 ml., S. C., of epinephrine; see above under anaphylactoid reaction) and allergic reactions (see above). Quinine hydrochloride and urethan can also produce an allergic reaction.

Shock.—Primary: Primary, or medical, shock is a temporary depression of the sensorium resulting from extreme emotion, fear, pain, disagreeable sights, or tragic news. The circulatory disturbances are temporary, and recovery is spontaneous and usually prompt. Occasionally syncope or fainting develops (see above).

Secondary or Surgical or Traumatic Shock: This is a severe disturbance of body function resulting from escape of blood plasma because of increased capillary permeability, loss of vasomotor tone with the consequent pooling of blood in the abdominal viscera, and/or loss of plasma or other body fluid or electrolyte. The result is a failure of cardiac output, fall in blood pressure, and the development of hypoxia leading to myocardial and central nervous system impairment and damage.

Signs: These are prostration, ashen color, circumoral pallor, thready pulse, and shallow respiration, but the patient is usually conscious.

Therapy: Maintain or restore blood volume preferably with whole blood or with plasma. Use shock position with head down and keep the patient warm with blankets. Cardiac and circulatory stimulants and vasomotor constrictor drugs are not of value either early or late and may be harmful. Oxygen by face mask is of some value in severe shock.

Nitritoid Crisis.—The nitritoid crisis is an idiosyncrasy of the person producing an

immediate reaction upon the injection of substances such as arsphenamines.

Signs: These are a choking sensation, palpitation, flushing of the face and neck, and injection of the conjunctiva. There may be edema of lips and tongue, a sense of suffocation and impending death, and symptoms of secondary (surgical) shock.

Improperly prepared arsphenamines may produce immediate violent illness with a sense of oppression and pain in the chest prior to collapse. The phenomenon is produced by pulmonary emboli with resultant pulmonary edema.

Therapy: Therapy of the nitritoid crisis is the immediate injection of 0.5 ml. of 1:1,000 epinephrine subcutaneously and more as later indicated.

Prophylactic Management of Emergencies

An adequate history and suitable testing where indicated will eliminate the great majority of possible untoward reactions. It is worth while to instruct the nurse always to place the ampoule, vial, or bottle from which she filled a syringe on the tray with it and to ask every patient prior to injection if he has ever reacted unfavorably to any injection. Air, oil, and arsphenamine emboli, as well as epinephrine overdosage, allow no reasonable, effective office therapy except prophylaxis. Epinephrine 1:1,000 solution, a barbiturate in solution, and an intravenous corticosteroid solution should be in each treatment table at all times.

Anaphylactoid reactions are best avoided by testing suitable dilutions of all protein-containing materials in eye and/or skin. This is impossible with live vaccines and impractical with crude liver; however, in the face of a history of a reaction with liver a skin test should first be made.

With materials containing animal serum, such as tetanus and diphtheria antitoxins, which are usually equine, a preliminary intradermal injection of 0.1 ml. of a 1:10 dilution of the tetanus antitoxin or 0.02 ml. of a 1:10 dilution of the diphtheria antitoxin should be performed. Wheals and erythema developing at the site of injection within 30 minutes represent a definite contraindication to the further use of the material unless desensitization is first carried out. The ophthalmic test consists of placing one drop of a 1:10 dilution of the antitoxin into the lower conjunctival sac of one eye. The contraindication reaction of redness, dilatation of vessels, edema and swelling of the lids, itching and lacrimation of the eye will develop within fifteen minutes. A severe positive reaction should then be treated by washing the eye out with 1:1,000 epinephrine solution.

Pollen solutions should be scratch tested before injection. The dilution of the injection should be judged by the degree of the scratch response. Hormones can be checked intradermally.

Epinephrine and intravenous corticosteroid should always be at hand.

Allergic reactions may be obviated by careful history and scratch or intradermal testing when in doubt.

For the primary immunization of persons over 10 years of age against diphtheria, a Schick test should first be performed. Schick reactors (positive) should then be tested for toxoid sensitivity by the intradermal injection of 0.1 ml. of a 1:100 dilution of plain diphtheria toxoid. If there is no reaction in 48 hours, one may proceed.

Local anesthetic toxic absorption reactions can be prevented in most cases by using a total dose which is less than the recommended maximum single dose for local infiltration. Some suggested limits are as follows: procaine hydrochloride, (Novocain) 1.0%, 100 ml.; piperocaine (Metycaine) hydrochloride, 0.5%, 75 ml.; and hexylcaine (Cyclaine) hydrochloride, 1.0%, 15 ml.

Nembutal sodium intravenous solution or other injectable barbiturates should be immediately available.

Epinephrine should not be used in local anesthetic solutions when they are used for the injection of digits because of the hazard of prolonged arteriolar spasm.

Epileptic seizures are best avoided by an extra dose of the patient's usual control medication before traumatic procedures. Given a history of seizures without medication control, it is best to refer the patient for this care. When this is not possible, 125 mg. of diphenylhydantoin (Dilantin) sodium may be given subcutaneously, or 3 grains (180 mg.) of secobarbital (Seconal) sodium orally one half hour prior to the intended procedure.

Syncope can frequently be prevented by not permitting patients to see instruments, needles, and procedures. Having all patients lie down before all procedures and injections is generally a worthwhile precaution.

Nitritoid crisis, once having been in evidence, is likely to occur with subsequent injections. It is stated that 0.5 ml. of epinephrine hydrochloride in 1:1,000 solution may be given subcutaneously prior to the arsphenamine to prevent the reaction, but I believe that once these symptoms have been seen the use of an arsphenamine should be totally abandoned.

Prevention of the embolic-pulmonary edema phenomenon is the cautious preparation and neutralizing of old arsphenamine used fresh. Neoarsphenamine preparations must not be allowed to stand and oxidize.

Drugs Involved in Emergency Treatment

Epinephrine Hydrochloride.—This is best used in a 1:1,000 solution. The intravenous route is rarely employed. The average adult subcutaneous dose is 0.2 to 0.5 ml. (0.2 to 0.5 mg.). Absorption may be hastened by vigorous massage of the injection site. The drug is contraindicated in secondary (surgical) shock and convulsive phenomenon. Diluted 1:2,000 to 1:50,000 it is of value topically in the control of hemorrhage from capillaries and arterioles, but there is no rational for its systemic administration in internal hemorrhage. Excessive doses may lead to ventricular fibrillation or cerebral hemorrhage.

It is available in an emergency Syrette (self-contained ampoule with a needle attached to it) packed under pressure so that bending the latex tube between the ampoule and needle breaks the ampoule and immediately injects the epinephrine solution.

Pentobarbital Sodium.—This is available in 5 ml. ampoules of sterile solution containing 0.25 gm. of the chemical (5% solution). This solution is ready for immediate intravenous injection. Thiopental (Pentothal) sodium has the disadvantage that it must be diluted before use. The initial average emergency adult dose of this pentobarbital solution is 2 ml. (50 mg. [¾ grain]) intravenously. One should then wait at least one minute to observe the effect while holding the needle in the vein. Then give additional fractional 1 ml. or less doses as required. For children and feeble adults the above dosage schedule should be cut in half.

In general the total dose should never exceed 10 ml. (0.5 gm.) except in a desperate effort to save life. When this maximum dose has not diminished the convulsions there is little possibility that more will be advantageous.

Amobarbital (Amytal), and secobarbital sodium are satisfactory alternates.

Corticosteroid.—Hydrocortisone sodium succinate (Solu-Cortef) is available in 100 mg. and 250 mg. "mix-o-vial" immediately available for intravenous injection. The product is stable for over one year and is replaced upon its anniversary without charge by the manufacturer. It is of distinct value in the management of anaphylactoid reactions, laryngeal edema, and precipitated asthmatic attacks. In the former two reactions it has a potentiating effect on the epinephrine which probably should be used first. Finally, it is said to be of value in surgical shock; 100 mg. (1.8 ml.) should be given intravenously immediately, and additional amounts as indicated.

Prednisolone 21-phosphate (Hydeltrasol), available in 40 and 100 mg. ampoules in buffered solution suitable for immediate intravenous injection, is also available and is said to be stable for one year. Give 20 to

40 mg. stat., I. V. and repeat as indicated. It is worth while to keep one of these in each treatment table at all times.

Crude Liver Extract.—This occasionally produces an anaphylactoid reaction. Pain and tenderness at the site of injection, together with faintness and flushing of the upper part of the body are all too common. Occasionally, fever and local induration develop and may persist for a few days. When liver is mandatory, as in pernicious anemia, the injections should be continued in spite of these lesser reactions because they usually disappear in a few weeks. The urticara, angioneurotic, idiosyncratic phenomenon are more apt to occur after the course of liver therapy has been interrupted for two or more weeks. Small doses (0.125 ml.) [3] given at 30- to 60-minute intervals are said to obviate serious reactions. Changing brands is not as valuable as once supposed. There is some evidence to indicate that the offending ingredient is usually common in the product of all manufacturers. Most commercial material is extracted from pig and cow livers. Changing to horse liver extract may be of some value. Some reactions may be the result of the inadvertent entry of the needle into a small blood vessel.

The allergic reaction component with crude liver can be avoided on repeat injections by not allowing more than five to seven days to elapse between injections. The dark liver extract makes the visualization of blood on syringe "pull back" difficult; therefore, it is better to use a glass-tipped syringe in distinction to the Leur-Lock type and to pull back until a tiny clear air bubble can be seen at the glass neck.

Conclusion

Should there be any doubt in differential diagnosis of the signs in an emergency, inject intravenously 100 mg. of hydrocortisone sodium succinate. It will do no harm; it will help in the great majority of emergencies; and it will permit further time to differentiate.

Summary

The important points to remember in a guide for extreme emergency are supine posture, patent airway, proximal tourniquet, and constant attendance. A guide to therapy is as follows:

Reaction	Therapy
Anaphylactoid	Epinephrine (1:1,000) 0.2-0.5 ml., S. C. Corticosteroid I. V.
Allergic	Epinephrine (1:1,000) 0.2-0.5 ml., S. C. Corticosteroid I. V.
Local anesthetic	Pentobarbital (Nembutal) 5%, 2 ml., I. V.
Epileptic seizure	Pentobarbital 5%, 2 ml., I. V.
Syncope	Smelling salts (ammonia)
Sclerosing solution	Epinephrine (1:1,000) 0.2-0.5 ml., S. C.
Acid spilled (bi- or trichloracetic)	Alkali (0.5% NaOH, $NaHCO_3$, or soap)

Solutions of epinephrine (1:1,000), barbiturate, corticosteroid, and a syringe with needle should always be immediately available.

1514 Anacapa St.

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Synthetic Detergents and Eczematous Hand Eruptions

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I. Background

The term "eczematous dermatitis of the hands" or "hand eczema" will be used here in the widest possible sense, namely, embracing all kinds of dermoepidermitides on hands and fingers with spongiosis in the epidermis. This is a heterogeneous group, including at least two very different diseases, contact dermatitis and atopic dermatitis, which periodically may be restricted to hands and fingers. The definition also includes "nummular eczema," regarded by many as a separate entity, distinct from both contact and atopic dermatitis, and sometimes suspected of being of microbic origin. There is, furthermore, the difficult question whether to include here the dysidrosiform eruptions of the palmar surfaces and side surfaces of fingers. Clinically, dysidrosis, of course, is very different from eczematous changes in other regions. However, microscopically they display spongiosis and are often associated with eczematous changes of the dorsal surfaces. One school of thought maintains that dysidrosis is a part of the atopic constitution; others believe that functional hyperidrosis is the primary pathogenetic factor, and, finally, some of us hold the view that dysidrosis may be a manifestation of contact dermatitis. An excellent review on eczematous dermatitis of the hands, causative factors, clinical manifestations and treatment, was published by Sulzberger and Baer in 1948.[1]

There is a widespread belief that synthetic detergents have a great potentiality to irritate the skin, greater than conventional soaps have.

Both soaps and detergents are known to be poor sensitizers.[2,3] Concerning primary irritating action in acute or chronic usage, there are no reliable observations in the literature which would definitely prove the irritating action of detergents as commonly used.

In our experience irritation by detergents does occur if the detergent solution is permitted to remain and become concentrated on the skin surface, as may happen under rings or if during the dish-washing procedure the dishes are held tightly for a considerable period of time in the detergent-moistened hand. Figure 1 shows the picture of a patient in whom the ring dermatitis could be produced at will by having her wash dishes with certain detergents and not others. Such dermatitis developed after a single dish-washing period and subsided in four days. The patient had no dermatitis

Fig. 1.—"Ring dermatitis" after the use of detergents.

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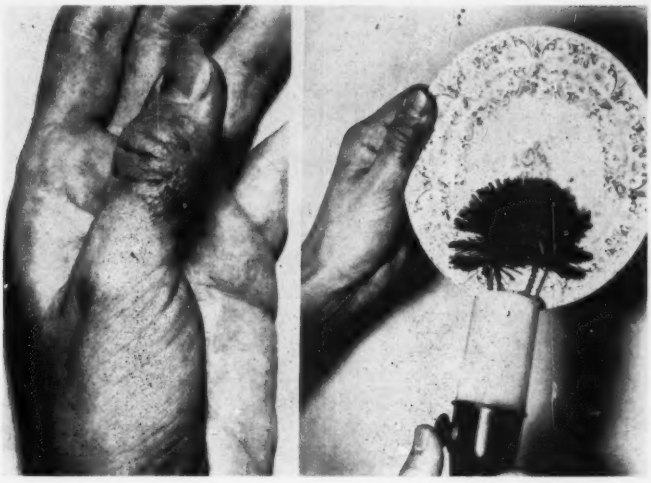

Fig. 2.—Eczematous dermatitis after repeated contact with detergents.

when she washed dishes without the ring on the finger. The ring had a hollow under the diamond setting, and detergent material accumulated in this hollow. Patch tests in this patient with filings of the ring material were negative.

Figure 2 shows eczematous changes on the left thumb of a housewife in the area in contact with the dish and close by. This woman used for a brush a spurting contraption. The undiluted strong soap solution hit the involved area at each spurt. This woman, too, was free of her eczema when she did not wash dishes.

Such findings, however, seem to be restricted to those instances where the skin is in contact with highly concentrated detergent solutions and for a considerable length of time. There is no evidence that in this respect modern detergents are more irritating than conventional soaps.

Dermatologists probably are unanimous in their opinion that exposure of the skin to water, soaps, and synthetic detergents, alone or combined, has its limits beyond which damage will necessarily result. The limit is highly variable individually and according to traumatic and other environmental influences. The limit is reached much faster in winter than in summer. Beyond the limit the horny layer and subcorneal barrier becomes damaged and secondary inflammatory reactions follow.

A fairly large set of both clinical and experimental data indicate that under regular usage conditions modern detergent solutions are essentially harmless for the skin of the hands, "essentially harmless" meaning that damage is rare and in most cases negligible and not greater than is attributable to conventional soaps. Foremost among these data are the interim and final reports of the Committee on Synthetic Detergents of the Ministry of Housing and Local Government of Great Britain.[4,5] In these reports of the British Government, it is stated that "experiments on men and animals indicate that irritation of the skin under conditions of normal use is relatively slight" and that "the incidence of dermatitis is not significantly greater than it was when soap and alkalies were the only common washing products." The reports say that inquiries made by the British Launderers' Research Association have not revealed any significant increase in dermatitis among laundry workers since modern synthetic detergents were introduced. Also, according to the report, the experience of manufacturers of detergents has been that in their own employees who have frequent and prolonged contact with synthetic detergents no

abnormal incidence of dermatitis has arisen. Inquiries with consultant dermatologists of the Ministry and with their divisional offices in close touch with general practitioners have shown that among the general population there has been some but no considerable incidence of such cases, many of which may have been due to the use of unnecessarily strong detergent solutions. The final conclusion of this report has been, "though many of the synthetic detergents now in use can and do give rise to skin irritation, more especially in predisposed persons, the individuals so affected are few, and in all probability not more than those previously affected by using other kinds of wash products."

In Germany, one of the foremost experts in the field, A. Szakall, in his recent monograph on the effect of washing products on the skin, published in cooperation with H. Stuepel, in 1957,[6] comes to similar conclusions. Among other data he quotes those of H. P. Kaufman who, working in the Dermatology Clinic of Muenster, found some of the finest conventional toilet soaps harsher on the skin than an American-made synthetic detergent.

In this country extensive studies have been carried out for many years on the effects of synthetic detergents on the skin in animal experiments and in man by diverse techniques of patch testing, by immersion techniques, and by tests "in the field" involving distribution of wash products to huge numbers of housewives who return at regular intervals for thorough examination of the skin of their hands by expert dermatologists. The same housewives have been given different wash products in successive time periods for comparative purposes.[7-9] The dimensions and organizational skill in performing this work have been indeed impressive. Among other achievements such studies have proved to be useful in the testing of new products for their skin-irritating properties in advance of marketing, so that some new products could be eliminated prophylactically when they proved to be too harsh on the skin.

It has been shown the detergents cause denaturation of keratins,[10] and this change may well decrease local protection. In addition, the forceful removal of lipids from the horny layer by defatting agents, such as soaps and detergents, contributes to the damage. According to modern research, even more important is the removal of water-extractable small-molecular substances, mainly amino acids, whereby the water-holding capacity of the horny layer decreases.[11-14] If the damage caused by denaturation and leaching-out reaches the subcorneal barrier membrane,[6] the whole epidermis becomes involved and its permeability increases to such a degree as to permit permeation of even the largest molecules and molecular aggregates, among them irritants and even microbes.

Although differences have been noted in the irritating properties of various wash products, there has not been much correlation with their defatting efficiency.[15] Disturbance of Marchionini's "acid mantle" [16] by alkaline wash products is probably not a major factor because of the excellent buffering capacity of the skin.[17]

We have been interested in the question as to whether by the use of modern synthetic detergents the limit of skin tolerance, as described above, is reached more easily than when only conventional soaps are used for washing. There has been an extremely rapid spread in the use of synthetic detergents in households and cleaning establishments after World War II. In the United States the use of synthetic detergents yearly increased from less than 1 lb. per person in 1942 to almost 10 lb. per person in 1951.[7] Because of this colossal change occurring within 10 years, we thought that if there is a decisive difference between pathogenic effects of conventional soaps and those of synthetic detergents this should be reflected in a different incidence of "hand eczema" in the general population after the detergents have become the generally used wash products. It should be possible to discover

this increased incidence statistically if comparable populations of the early forties and early fifties are analyzed for the incidence of "hand eczema." Therefore, it was decided to compare the incidence of "hand eczema" at The University of Chicago Clinics in the years 1942 and 1943 with the incidence in 1952 and 1953. Such statistical work was expected to reveal whether among all persons who feel compelled to see a skin specialist the relative number of those who have "hand eczema" has increased in 1952-1953 as compared with 1942-1943. In addition to this statistical work, we attempted to question closely all patients with "hand eczema" we could reach for the possible etiologic role in their own judgment of soaps and detergents.

II. Methods

Statistical Analysis.—A total count was made of all adult patients, 16 years old or older, seen for the first time in the clinic, during the two two-year test periods. Subsequently the number of cases with the diagnosis of "hand eczema," including nummular eczema and dysidrosis, restricted to the hands, was counted in each period. Cases of dermatophytosis and dermatophytids were excluded. Male and female patients were counted separately.

We wanted to make it sure that our patient population in the 10-year interval had not shifted because of possible social and economic changes beyond the introduction of synthetic detergents. For instance, in our clinic it might have been possible that a great decrease in incidence of industrial dermatoses might have occurred because industrial workers are now being taken care of in greater numbers by company doctors. Or, an epidemic skin disease, such as tinea capitis in either of the two periods, may have shifted the relative incidence. We felt that the homogeneity of the populations in the two time periods can be best checked if we also count the incidence of psoriasis. Psoriasis was chosen as a control because we assumed it to be a disease independent of variable environmental influences, particularly independent of social, economic, external chemical, and internal metabolic factors and regarded it as a primarily genetically induced disease. If the incidence of psoriasis has shifted, independent of the shift in the incidence of "hand eczema," we cannot be sure that our population has remained stationary.

TABLE 1.—*Total Number and Sex Distribution of Patients Used in Statistical Analysis*

	1942-1943	1952-1953
Patients, no.	2,226	2,503
Males, no.	907 (40.8%)	1,057 (42%)
Females, no.	1,319 (59.2%)	1,446 (58%)

III. Results

1. *Results of Statistical Analysis.*—For the two two-year test periods a total of 4,729 adult patients (2,226 in 1942-1943 and 2,503 in 1952-1953) were admitted as new patients to the Dermatology Clinic and their records examined.

Tables 1-4 show the numbers of patients and percentages for the two two-year periods surveyed.

Table 2 indicates that the relative number of hand eczemas in females was considerably higher in the 1952-1953 period than a decade earlier, while there was no significant increase in males. The great increase in females was sufficient to cause a highly significant increase also in the incidence of hand eczema in the two sexes together. This great increase in females, and not in males, of course, strengthened the suspicion that the newly introduced deter-

TABLE 2.—*Incidence of "Hand Eczema"* *

"Hand Eczema"	1942-1943	1952-1953
Males	7.3% (67)	7.4% (79)
Females	5.3% (71)	9.0% (131)
Both sexes	6.2% (138)	8.0% (210)

* Expressed in percentages of total numbers of admissions; absolute numbers in parentheses.

TABLE 3.—*Incidence of Psoriasis* *

Psoriasis	1942-1943	1952-1953
Males	3.2% (29)	3.7% (40)
Females	2.0% (27)	3.2% (47)
Both sexes	2.5% (56)	3.0% (87)

* Incidence expressed in percentages of total numbers of admissions; absolute numbers in parentheses.

gents contribute to the elicitation of irritative dermatitides of the hands. However, in psoriasis there was again a significant increase of incidence in females without significant increase in the males.

The data were submitted for statistical analysis. Certainly, both changes, in female hand eczema and in female psoriasis, were statistically significant. The question, of course, arose whether the increase in "hand eczema" in females was significantly greater than the increase of psoriasis in females. Natural though this question was, we found out to our grief from the Chairman of our Department of Statistics, Dr. L. J. Savage, that its exact meaning is not clear. However, Dr. Savage gave us a good informal interpretation of the battery of statistical tests performed. He said, "The evidence for an increase of hand eczema rate in American women is about as substantial as a study of this limited sort and size could provide with the serious exception that the control of psoriasis is not as satisfying as might have been hoped." He added, "There is no strong evidence that the eczema effect is greater than the psoriasis effect apart from random fluctuations."

After completion of this statistical study, we encountered a pertinent finding of Hoede,[18] who, for 30 years, has been a student of genetics in psoriasis [19] and who has registered the records of 3,719 psoriatic patients. He finds that in recent years the incidence of psoriasis in females as compared with that in males has increased. Hoede believes that this change might be based on error of registrations, because the same females might have been registered twice as new patients, once by their maiden

TABLE 4.—*Sex Distribution of "Hand Eczema" and Psoriasis in 1942-1943 and 1952-1953*

	1942-1943, %	1952-1953, %
Total males	40.8	42
Total females	59.2	58
"Hand eczema"		
Participation of males	48.6	38
Participation of females	51.4	62
Psoriasis		
Participation of males	51.8	46
Participation of females	48.2	54

name and once by their married name. It is rather improbable that there has been a true world-wide tendency to a shift in sex distribution of psoriasis in favor of the female sex, but this is not entirely impossible. Before definite conclusions can be drawn on the possible increase in incidence of "hand eczema," another disease will have to be used as a control.

2. *Results of Interviews with Patients.*—(*a*) Out of a total of 348 patients with "hand eczema" (138 seen first in 1942-1943 and 210 seen first in 1952-1953), a total of 48 could be interviewed. Forty-six were from the 1952-1953 period and only two from the 1942-1943 period. There were 31 female and 17 male patients, 44 white and 4 Negro, in the age group from 25 to 66 years old.

Their original diagnoses are as follows:

1. Dysidrosis	33
2. "Housewife eczema"	7
3. Exudative neurodermatitis, restricted to hands	2
4. Dry neurodermatitis, restricted to hands	1
5. Contact dermatitis due to specific substances other than washday products	5

(*b*) Concerning the course of the "hand eczema," the following data were obtained in late 1955 (at least two full years after the first visit):

Continuously present & no change	10
Continuously present but now better	15
Present & better with history of remissions	11
Absent with history of recurrences & remissions	8
Completely absent for 6 mo. or more	4

(*c*) Patients were thoroughly interrogated whether in their own opinion their "hand eczema" was or could have been

related to the use of washday products. The answers were as follows:

No relation	26
Not sure	5
Eczema was caused by detergents	3
Soap and/or detergents made the eczema worse	14

(*d*) Patients were questioned on the factors which in their opinion made their "hand eczema" worse. The answers to these questions were as follows:

Nervousness	23
Washday products	17
(out of these, specifically detergents & not soap or water, 5)	
Water (especially hot water)	11
Environmental heat	10
Industrial contacts	6
Other exogenous contacts	6
(out of these, contact with food material, 3)	
Cold	2
Menses	1
Eating certain foods	1
Systemic medication	2

(*e*) Questions concerning exposures to wash-products, their intensity and duration, and concerning the possible protective action of rubber gloves did not yield any conclusive results. With the limited numbers involved there was no way of relating the numbers who used rubber gloves when doing wet work (27 out of 48) to the numbers who improved. On the whole, the patients who did not use gloves were those with the milder form of disease or those who had limited contact with wet work. Improvement was about evenly divided between those who did a great deal of housework and those who did not. Of course, the main difficulty in evaluation has been that only four patients seemed to have cleared permanently. It might be worth while to mention that out of 35 patients who washed dishes regularly when the hand eruption appeared only one has completely ceased to do such work.

(*f*) Answers to miscellaneous questions were as follows:

1. Nineteen patients noticed chapping ("dishpan hands").
2. Twenty patients never wore rings (fifteen wore rings and felt they made no difference in the course of eruption; thirteen said wearing rings made worse or the eruption was first seen under their rings).
3. Nineteen felt that hands and/or feet sweat excessively.
4. In 13 the eruption had always been restricted to the hands, and in these patients there was no history of any other skin disease.
5. Fifteen had had eruption spread from hands to forearms at some time.
6. Eight had had some kind of generalized skin eruption (excluding exanthematous childhood diseases) in the past.

IV. Comment

The figures tend to indicate that there definitely has been an increase in hand eczema in women. However, a simultaneous increase of psoriasis in women makes the results difficult to interpret. Of course, a study such as this is further limited by the restricted population dealt with, and such a population might vary in a manner not absolutely reflecting the trends in the population as a whole. Furthermore, although we may be justified in concluding that hand eczema has increased in women in recent years, we certainly cannot be sure how much, if any, part in this the new synthetic detergents have played. Vast changes have occurred in our way of life since World War II. A number of irritating substances other than washing products are daily encountered by the modern housewife. Nevertheless, it is interesting to note that, within the limits of this study, there has been no increase in the incidence of hand eczema or psoriasis in men.

Many hand eczemas tend to be chronic or recurrent and emotional stress appears to play a role probably primarily via emotional hyperidrosis. Other factors, such as hot water alone, soaps and detergents, heat, and industrial and other contacts (food, cleaning solution, etc.) often aggravate the condition. There is occasionally a spread of the eruption to other areas, especially the forearms. The hyperidrosis frequently seen in these patients undoubtedly has a deleterious effect. Slightly less than one-half of our patients who wore rings had noticed that the eruption first appeared under the ring or was worse in this area as long as the ring was worn.

At the present time it is impossible to say whether the every day use of the new synthetic wash-day products is harmful to the hands or whether or not the new products are any worse or as bad as the old strong soaps. The synthetic detergent preparations as well as soap and water appear clinically to aggravate hand eczema.

Summary

An increase in eczematous dermatitis of the hands in females in a clinic population has been noted between the early 1940's and the early 1950's. While this increase has been statistically significant, the interpretation of the data could be questioned because in the same material and at the same time an increased incidence of psoriasis in females also was found. The disease of the hands tends to be recurrent, and nervousness probably via emotional hyperidrosis appears to be of great importance in precipitating the eruption, although a number of other factors are certainly contributory.

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ABSTRACTS OF DISCUSSION

DR. CLINTON W. LANE, St. Louis: It is always a pleasure to discuss a paper of Dr. Rothman because his subject is so completely covered and his conclusions so well justified that there is little for a discusser to add. My remarks will consist of raising a few questions which seem pertinent and possibly offer some slight differences of opinion.

It has been the belief of many observers, including myself, that inflammatory eruptions of the hands are observed much more often at present than they were 10 and 20 years ago.

In checking over office records, there was a close correlation between the figures obtained in the clinic of Dr. Rothman and those in private practice. The proportion of males observed by us was 43% in 1942 and 42% in 1952, while, in 1942, females comprised 57% and 58% in 1952. It had always seemed that women made up a much higher percentage than men (possibly due to their more numerous questions and the more difficult management problems). While the incidence of hand dermatitis in the two periods was almost identical in men, there was a 7% increase in women in our practice.

That this increase can in part be attributed to detergents seems plausible. In our experience, there was more hand eczema in women during the winter months than the summer because of harshness and dryness of the skin with resultant increased susceptibility to irritation. Soaps and detergents contribute to this increased dryness, but detergents, being better wetting agents than soap, are, therefore, better defatting agents. Also, some detergents are reinforced by alkalies such as phosphate and sodium carbonate, which increase their potential as drying and irritating agents.

Dr. Rothman has shown that in a 10-year period there was a significant increase in eczematous hand eruptions in women but little change in the increase in men. The period of 1942-1943 was during the war years, when many women were employed in industries in which their hands were exposed to new substances. Many of these materials were potential irritants, and some, like oil and grease, required the use of strong cleansing agents for their removal. One would suspect that female hands at that time would have a higher incidence of eruption than in 1952, all other things being equal.

In our modern mode of living, there are more electric and automatic washing machines, electric dryers, and dishwashers than in 1942. Doubtless, these keep more women's hands out of soap and water, and, if there is an increased incidence of hand dermatitis now, one should look elsewhere for the cause. A reasonable assumption is that detergents are the offenders.

Hyperidrosis and dysidrosis are important factors in the incidence of hand eruptions. Some dermatologists and many patients believe these phenomena have a psychogenic basis. Admitting that there were numerous causes of stress and nervousness in 1952, they should not approximate the tension of the women in 1942, some of whom were employed in new, nerve-wracking jobs, and many of whom had husbands, relatives, or friends away from home in the armed services. It would seem that female hand eruptions of this type in 1942 should have been more numerous than similar eruptions in 1952 unless there was some other cause in the latter period.

In private practice, the incidence of psoriasis in male and female patients did not vary more than 1% in the same years in which Dr. Rothman obtained his figures, and they are the same in the year 1957. It might be of valuable interest if some other dermatoses, such as lichen planus, erythema multiforme, or, preferably, seborrhea were to be tabulated to see if they conformed to his eczema-psoriasis pattern.

In Dr. Rothman's tables, there was a higher percentage of male patients in the clinic and fewer females in 1952 than in 1942. Since psoriasis and hand dermatitis were seen more frequently in the females, were there other dermatoses with a lower incidence or did men have some type of eruption more often in 1952? This is not directly related to the present discussion but should yield much pertinent information.

It has been a real pleasure to read and hear Dr. Rothman's excellent paper, and, although it is outside the scope of this discussion, it is to be hoped that in the future he will offer, not only a cure, but even more important, effective, preventive measures for these resistant exasperating hand dermatitides.

Dr. Roy L. Kile, Cincinnati: I come from a city that probably has the largest detergent-manufacturing plant in the world. Being around this environment both from the standpoint of treating the employees and in contact with the biochemists who are working in their research department, I have managed to pick up a little information about this tremendous and growing problem.

If it is true that the use of detergents has increased dermatitis of the hands, then we are going to see a lot more of it because the use of detergents is growing so rapidly that before long soap will not be available for heavy-duty use. Practically all shampoos are now detergents, and very gradually detergents are creeping into the field of toilet soaps. Detergents are also being used for many other things, as, for example, their recent employment as cathartics.

It has always been my feeling that detergents defat the skin and thereby open the avenues for infection. I feel that many of these hand eruptions are infections that are merely aggravated by the use of detergents just as we saw them aggravated by the use of stronger soaps back in the days long before detergents were available. Also, many of these cases fall in the group of erythema multiforme, for I have seen these cases definitely get worse in the fall and spring as is so common with erythema multiforme. There is also the fact that when they spread up the arms or over the body typical iris-like lesions often develop.

The problem of ring dermatitis is an interesting and fascinating subject. Dr. Gaul, of Evansville, Ind., at one time felt that trauma from rings was an important factor. I noticed that he recently has suggested a chemical in the sweat may react with the metal in the ring. There are many possibilities. I do not believe any of us are sure at the present time what it is. Here again I think infection is an important problem and all of us have seen this ring dermatitis spread to produce a typical eruption generalized over the hands.

I think a very interesting facet of this problem, although not directly related to the subject under discussion, is the marked decrease in scabies in recent years. It has almost come to the point where we do not even consider scabies in differential diagnosis anymore. What effect have synthetic detergents had on this problem of scabies? Why the marked decrease in recent years?

At the present time at the Cincinnati General Hospital there is a study going on, under the direction of Dr. Leon Goldman, in which they have shown that soaking the hands in detergents by women with hand dermatitis does not make them worse. Actually, some of them improved while they were applying wet packs of detergent solutions. I do not know how significant this study is from a practical standpoint. I imagine there will be further publications regarding this line of study that they are doing. I do not, by any means, mean to infer that detergents are completely harmless, for I think they aggravate a number of existing skin eruptions. Just as they do a good job of cleaning, so they also remove oil and grease from the skin. By the same token, however, I feel that detergents have been unjustly blamed for many skin eruptions.

Dr. Adolph Rostenberg Jr., Chicago: It seems that life is getting increasingly hazardous, not only from the point of view of ionizing radiation but also from the standpoint of eczematogenous substances. Dr. Rothman's paper is, in a sense, a facet of a larger problem of the interrelationships between primary irritation and subsequent eczematous processes, and vice versa.

A few years ago, in a paper before the Academy, I reviewed some of these factors. I was surprised at the paucity of information about the influence of one primary irritant reaction upon a subsequent one or upon a subsequent eczematous sensitization, or the reverse. As a matter of fact, we really know nothing about the pathogenesis of primary irritant reactions. We know, of course, this is, possibly, the commonest of all dermatological conditions; yet, the true means by which it comes about is not known.

Dr. Kile has intimated or stated one of the things. I wanted to say, namely, that experimentally there is not much evidence that a primary irritation predisposes to subsequent primary irritations. Jambor, under the conditions of his experiment, failed to find that soap solutions irritated an eczematous process. Haeberlin, Oliver, and myself, some years ago, repeated patch tests with primary irritants. We were unable to show that there was any discernible extra irritation from repeating a primary irritant; that is, placing a primary irritant on the site of previous primary irritant.

Certainly, from the clinical point of view, all of this is nonsense. I think that all of us would strongly feel that a primary irritant would add to an existing dermatitis, and I certainly feel that. I think what it does show is that this is a very complicated issue and that one has to segregate all the factors very carefully. The time relationships in these experiments are very important. The question of concomitant friction and the nature of the irritants used are also important.

Next month it will be 25 years since I have been in dermatology, and I do not know whether I know more about less and less or less about more and more.

Dr. Herbert S. Alden, Atlanta: This sort of paper on hand eczema brings up, of course, a great many conflicting points among all of us. I should like to remind Dr. Rothman that if he will have his housewife take off her ring, he will find a depression in the back of the ring. If he will place a little piece of onion, or a little piece of garlic, or, for that matter,

almost any vegetable, in that ring, and put it back on the finger for a few hours, it will be a satisfactory patch test. Most eczemas in housewives that I see usually begin under the ring finger.

DR. RUDOLF L. BAER, New York: When I read the abstract of Dr. Rothman's excellent paper, I inquired of one of the large soap manufacturers whether figures are available regarding the comparative number of complaints about a synthetic detergent and a household soap received during the same one-year period. The records of this manufacturer indicated that the number of complaints received from users of a so-called heavy-duty soap and a heavy-duty detergent during the same one-year period in 1955 were practically identical per 1,000,000 cases sold. Thus, there was no indication that synthetic detergents caused a greater incidence of dermatitis than soaps.

It is of interest, however, that some of these synthetic detergents exert effects which indirectly may lead to irritation. I should like to call your attention to the work of Nilzen and Wikstrom (*Acta dermat.-venereol.* 35:292, 1955), who were able to show in the guinea pig that nickel sulfate and chrome, substances which under ordinary circumstances are incapable of producing allergic sensitization in guinea pig's skin, readily produced such sensitization when applied together with sodium lauryl sulfate, a synthetic detergent. Therefore, one must consider the possibility that in man, also, certain synthetic detergents might well be pacemakers for allergic sensitization to agents to which the hands are exposed. Another effect which must be kept in mind with respect to possible side-effects of synthetic detergents is their acanthogenic action. This, as we have been able to show at least in experimental animals, appears to have a significant effect on the capacity of the skin to respond to allergens and primary irritants.

DR. JOHN G. DOWNING, Boston: The late Paul O'Leary once remarked that hand eruptions were intriguing but also disappointing for prolonged study and that they were nothing but ham and eggs. However, to the practicing dermatologist, like ham and eggs, they are very sustaining, and results must be obtained because they are very disabling to the patient. Hand eruptions comprise the bulk of a busy practice.

The causative factors must be eliminated in order to give complete relief. Years ago, with fewer contacts, the cause was fairly easy to ascertain. For one housewife, it could be preparing tomatoes for the fall canning; for another, perhaps the skin of citrus fruits; even the dermatitis of hairdressers would be eliminated by testing them with their contacts, which were less numerous than the present-day products.

However, today, with the vast number of new chemicals, such as detergents, waxs, and solvents, introduced not only into the homes but also into industries, patch testing reveals so many possibilities that we now realize that it is not one or two factors but a combination of many.

I believe that with the housewives and workers doing wet work, the detergents play a large part, for there has been a definite increase in the use of these products with the housewives since they have been introduced, as they lighten household activities considerably. The eruptions generally start under the woman's rings and spread to the rest of her hand. The eruptions continue as long as there is contact with the detergent.

I believe the increase of psoriatic eruptions of the hands may be due to the Koebner phenomena as a result of continued irritation.

DR. STEPHEN ROTHMAN, Chicago (closing): First of all, I should like to state emphatically that I did not say that synthetic detergents do not damage the hands. I wanted to investigate the problem objectively. With all respect to Dr. Downing's great practical experience, I am just not satisfied with hearing, and I quote, "I am convinced there is an increase, and that this increase is due to detergents." I wanted to find out about it in an objective way, with statistical work. I fully agree with Dr. Lane that it might have been a mistake that we took psoriasis as a control. We should have taken, maybe, warts or lichen planus or acne or something else, because psoriasis did not prove to be a good control. I plan to do this. But as long as I do not see quite definite statistical proof that this increase of hand eczema in females is statistically valid, I shall withhold judgment on the matter.

As far as the war years are concerned, I should like to call attention, Dr. Lane, to the fact that since the war years, in addition to the new detergents, there have been other cleansing agents in the kitchen and in the household which have become more caustic than they were before. So, perhaps, the increase in dermatitis of the hands may be due not only to synthetic detergents but to other chemicals as well.

Dr. Lane and Dr. Kile mentioned defatting. When I started my study, I was convinced, too, that forceful defatting is harmful. I am not so absolutely convinced today. I am convinced that the detergents are harmful if used in extreme concentrations. I am not absolutely convinced that they are harmful in normal usage. Of course, they are pacemakers, as Dr. Baer pointed out, but they may be pacemakers only when they are used in higher concentrations than required in normal usage. In high concentrations they may break the subcorneal barrier.

My impression has been that the great majority of complaints on so-called detergent burns come in from crackpots or people who are incited by lawyers to make a suit. The famous suits have all been based on absurd claims, which, of course, does not mean that detergents do not hurt the skin.

I should like to make it clear that I do not know, but my personal feeling is that detergents are more harmful for the hands than the old types of soap, and I just wanted to state that I could not prove this. I am not satisfied just with feeling or with conviction, without having definite proof of it. I certainly have great misgivings about the inscription on the boxes, that "this is harsh on the dish and mild on the hands," because if it is harsh on the dish, it is probably harsh on the hands, too.

Generalized Flushing of the Skin with Urticaria Pigmentosa

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In 1869, Nettleship [1] described an unusual type of urticaria which bears the name urticaria pigmentosa. For the next 80 years it was regarded as a comparatively rare skin condition characterized by yellow or brown macules or nodules, which, when rubbed vigorously, produced a whealing or urtication localized to the pigmented areas. Apart from the occasional report of rare solitary nodular and bullous lesions, the only other significant observation during this period was the finding of Unna,[2] in 1887, that the skin manifestations of urticaria pigmentosa were characterized by a marked infiltrate of tissue mast cells.

In 1949, Ellis [3] reported the first case of urticaria pigmentosa in which an autopsy was performed. This one-year-old Negro girl had the typical skin lesions of urticaria pigmentosa from birth, associated with gastrointestinal upsets and hepatosplenomegaly. The autopsy revealed increased numbers of mast cells in the areas of portal cirrhosis of the liver and in the spleen, kidney, lymph nodes, periadrenal fat, pancreas, and endosteum of bone, as well as in the skin. Since that time, several cases of urticaria pigmentosa with visceral involvement have been reported and several others with leukemic or leukemoid changes in the blood. Nickel [4] recently summarized these reports in an excellent article.

In 1952, Sagher et al.[5] and Clyman and Rein [6] reported bone lesions associated with urticaria pigmentosa and Sagher established a central registry in Jerusalem for bizarre types of the disease. Of the 52 cases [7] which have come to his attention, more than one-third have had some type of osseous lesions. The bone lesions may take the form of (1) generalized osteoporotic and osteosclerotic areas or (2) similar areas confined mainly to the skull, femur, and humerus. At postmortem examination, mast-cell accumulations have been found in the marrow of the affected bones.

With the recent recognition of the possible widespread nature of this disease there is an increasing tendency to call the condition mastocytosis, and the solitary nodular lesions, mastocytomas. There has also been a renewed interest in the nature of the mast cell and its function. Tissue mast cells are connective tissue cells of the histiocyte family whose cytoplasm contains granules which stain metachromatically with toludine blue and certain other basic dyes. It is thought that the tissue mast cell has nothing in common with the blood basophil except the basophilic metachromatic staining of the granules in the cytoplasm. Many physiologic properties have been attributed to the tissue mast cell, and Fulton et al.[8] summarize them when they suggest that mast cells are like unicellular endocrines which produce (1) heparin, (2) hyaluronic acid, (3) histamine, and (4) serotonin (5-hydroxytryptamine). It has not been conclusively proven whether these substances are produced, or only stored, in the mast cells.

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Presented at the 50th Annual Meeting of the Manitoba Medical Association, Oct. 9, 1958. The three cases reported were shown at a meeting of the Minnesota Dermatological Society held in Winnipeg, Sept. 15, 1957.

It is the purpose of this paper to present two cases of solitary nodular bullous urticaria pigmentosa and one of generalized macular urticaria pigmentosa occurring in children and accompanied by the uncommon finding of generalized flushing of the skin.

Report of Cases

CASE 1.—This patient was a baby boy, aged 5 months, with a solitary lesion on the dorsal surface of his left hand since 1½ months of age. His mother stated that the mark "goes up and down." Since sleeping that afternoon, it had become blistered, though there was no history of a burn or unusual trauma. The lesion (Fig. 1) was about 2 cm. in diameter, the skin was slightly raised and firm and was yellowish-brown in color and surmounted by tense tan-colored bulla. The blood cell count was normal, and roentgenological skeletal survey did not reveal any bony abnormality. The hand was kept bandaged for the next six weeks until the blister had completely subsided and the lesion had taken on the appearance of a smooth yellow-brown plaque. At that time, the lesion was rubbed vigorously to try to produce whealing and confirm the diagnosis of urticaria pigmentosa. Within the first minute of observation, the mother exclaimed, "Look, there he goes now." The child started to cry and developed a blotchy red macular flush that started at the top of the head and spread down over the face, chest, and back. It faded within a few minutes. A wheal appeared at the site of the rubbing of the pigmented lesion on the hand, and by the next day it had developed into a bulla. During the next year, an effort was made to keep the hand covered to protect it from friction. However, during that time, at intervals of about two months he was able to get the hand free and rub it. In each instance it was followed by a peculiar cry and flushing of the skin and subsequently by blister formation on the hand. If the lesion was rubbed while it was healing from these episodes nothing unusual could be observed to happen and there was no local whealing. Because this flushing disturbed the mother so much, the lesion was removed surgically six months ago. The microscopic examination showed an extensive accumulation of mast cells in the superficial and deeper layers of the corium (Figs. 2 and 3). There has been no recurrence of flushing since the operation.

CASE 2.—A baby girl, aged 4 months, had had a "birthmark" on her left thigh since the age of 1 week. The night before her first visit, she had developed a blister on the birthmark. On questioning, the mother stated that after her late afternoon feeding the baby broke out in a blotchy red rash that spread all over the body. It lasted for about five minutes and did not appear to bother the child. Three hours later, when the baby was being put to bed, the mother noticed the blister on the birthmark. The mark had never blistered before. The lesion was just below the crest of the ilium and consisted of a firm yellow plaque, about 2 cm. in diameter, surmounted by a very tense bulla full of straw-colored fluid. A blood cell count and roentgenological survey of the skeleton for bone defects was negative. Sixteen days later, when the blister had completely subsided, the lesion was rubbed vigorously with a blunt object (Fig. 4). Within one minute, the baby's face and the area surrounding the lesion on the thigh developed a blotchy red macular eruption. It gradually spread downward over the neck, shoulders, trunk, and thighs. It was symmetrically blotchy over the shoulders and trunk and left large white islands between the areas of red flushing (Figs. 5 and 6). The mother was amazed. The flush disappeared in the same order that it appeared and was gone within five minutes. It did not upset the baby in any obvious manner. No blister formed at the site of the lesion. Fortunately, we were able to take a moving picture of the whole reaction. The lesion was removed over one year ago. The microscopic section showed a heavy accumulation of mast cells and also appreciable numbers of eosinophils within the superficial and deeper layers of the corium. There has been no recurrence of flushing since the operation.

CASE 3.—A 3-year-old girl had had widespread macular urticaria pigmentosa on the trunk since 4 months of age. There was no history of skin flushing. The blood cell count was normal, and a roentgenological skeletal survey did not show any abnormalities. A biopsy specimen revealed the typical infiltrate of mast cells. Nine months later she developed a severe flush on her face, arms, and body while at Sunday school. It lasted one-half hour and was severe enough to send her home. The child had a cold at the time and had taken two

Fig. 1.—Solitary bullous lesion of urticaria pigmentosa on dorsal surface of hand.

Fig. 2.—Extensive accumulation of mast cells in the superficial and deeper layers of the corium.

Fig. 3.—Heavy accumulation of mast cells around a sweat gland.

Fig. 4.—Solitary nodular lesion of urticaria pigmentosa.

Figs. 5 and 6.—Erythematomacular flush most marked over face, shoulders, arms, and hips, initiated by rubbing solitary lesion over left hip.

Figs. 7 and 8.—Erythematomacular flush, most marked over face, shoulders, arms, and hips, initiated by the subcutaneous injection of codeine phosphate.

Figure 1

Figure 2

Figure 3

Figure 4

Figure 5

Figure 6

Figure 7

Figure 8

doses of a cough mixture containing codeine phosphate, ⅛ grain (8.1 mg.); ephedrine, 1/16 grain (4 mg.), and histadyl, ⅙ grain (10.8 mg.) per dose. As codeine belongs to the morphine-opium alkaloid group, it is a histamine releaser and could liberate histamine from mast cells. Two weeks later, when she was admitted to the hospital for a tonsillectomy, the opportunity was taken to give her an injection of the drug. Codeine phosphate, ¼ grain (16.3 mg.) was adminstered subcutaneously. In 15 minutes, a wheal appeared at the site of the injection and subsided within the next 15 minutes. One half hour after the injection, the scalp became bright red, and then a flush spread down over the face, shoulders, arms, thighs, and legs (Figs. 7 and 8). The eruption was blotchy and was exactly the same as that seen on the two previous cases. It lasted 45 minutes and faded in the same order that it appeared. There was no whealing at the sites of pigmentation, no respiratory distress, and no itchiness. The urine was examined for metabolites of serotonin.

Comment

Urticaria pigmentosa, occurring as a solitary nodular lesion, is a rare condition. Chargin and Sachs,[9] in 1954, stated that only 10 cases had been reported in the American literature to that time. Marshall et al.,[10] in 1957, listed an additional eight references, many of them French, and reported two cases of their own. Lynch [11] and Zackheim [12] have each cited cases, and Jacobs [13] published an interesting report of solitary lesions occurring in a mother and her daughter. To date, at least 24 cases have been recorded. The majority of these solitary nodular lesions have been associated with the formation of bullae at sometime during their course.

There have been very few reports of generalized flushing of the skin with urticaria pigmentosa. Marshall quotes Degos to the affect that Morrow recorded this phenomenon in 1879. It was not until 1947 that the next case was reported by Tavs,[14] a single episode of generalized flushing in a 2½-year-old girl with widespread urticaria pigmentosa and the formation of bullae. Including the cases cited by Marshall and the reports of Rider et al.[15] and Davis et al.,[16] 11 cases of flushing of the skin associated with widespread urticaria pigmentosa have been recorded.

Flushing of the skin with solitary mastocytoma is even more uncommon. We have been able to find only three recorded cases: the two reported by Marshall and his recording of an earlier case reported by Degos. In Marshall's cases, the generalized flushing and swelling of the mastocytoma were spontaneous and not induced. In the cases presented in this paper flushing was induced in two by mechanical irritation and in one by probable chemical stimulation of the mast cells. Morrow, in his original communication, and Marten [17] and Bowers [18] each noted the appearance of flushing of the skin after the lesions of widespread urticaria pigmentosa were handled. As far as we are able to ascertain, cutaneous flushing has never been induced before in this disease by the use of chemicals.

It is usually assumed that the whealing in urticaria pigmentosa is due to the release of histamine or histamine-like substances from the mast cells, and it might follow that the generalized flushing of the skin is due to the liberation of large amounts of histamine from concentrated depots in the skin. However, the flushing of the skin closely simulates that seen in the carcinoid syndrome. In this syndrome, functioning carcinoid tumors release 5-hydroxytryptamine (5-HT, serotonin) which produces flushing of the skin, and sometimes intestinal cramps, diarrhea, and respiratory distress. Its presence can be detected by finding abnormal amounts of 5-hydroxy-3-indolacetic acid (5-HIAA) in the urine. 5-Hydroxytryptamine is present in mast cells, and Benditt and Rowley [19] demonstrated that it is liberated from mast cells along with histamine by some "histamine liberators." It, therefore, could play a part in the cutaneous flushing of urticaria pigmentosa. In the cases recorded in this paper, there were no other signs or symptoms than the whealing at the site of stimulation and the generalized flushing. However, in the case reported by Dewar and Milne [20] repeated attacks of dyspnea

TABLE 1.—*Tissue Assays for Histamine and 5-Hydroxytryptamine*

Case, No.	Histamine, μg/Gm.	5-HT μg/Gm.
1	50	23
2	14	—
3	133	Trace

TABLE 2.—*Estimations on the Urine for 5-Hydroxy-3-Indoleacetic Acid* *

Case, No.	Control, Mg.	After Stimulus, Mg.
1	Trace	Trace
2	—	—
3	0.57	3.12

* 24 hr.

and cyanosis occurred, coinciding with fresh outcrops of vesicles and bullae; in Marten's patient, the attacks were accompanied by shivering and listlessness, and Rider's patient had abdominal pain, vomiting, and diarrhea. It is interesting to note that Lynch's patient had been investigated for convulsions, and that Dewar's patient had also been admitted to the hospital for the treatment for convulsions. All of these patients were children.

Table 1 shows the results of tissue assays for histamine and 5-HT in our patients. It is unusual that in Case 3, the child with the generalized urticaria pigmentosa, the histamine content was much higher than in the two with solitary mastocytomas. There is usually a close relationship between the mast-cell content and histamine value of tissue. Most reported values for urticaria pigmentosa vary between 20μg.-50μg. per gram, though Riley[21] found the unprecedented value of 950μg. per gram in a large solitary lesion. In case one the microscopic section was infiltrated with eosinophils, and this is usually interpreted to mean that the mast cells are in the process of disruption. It is possible that this patient was not examined when the mast cells were at their peak capacity. The periodicity of attacks, followed by refractory periods to stimulation, would tend to confirm this. The serotonin estimations on the tissue were essentially negative, and correspond to the findings of West and Parratt,[22] Davis et al.,[16] and Gardner and Tice.[23]

The results of estimations on the urine for 5-HIAA in Cases 1 and 3 are shown in Table 2. In making this examination, attention must be paid to the recent finding of Anderson et al.[24] that bananas contain 5-HT and that increases amounts of 5-HIAA can be found in the urine after the ingestion of bananas. The specimens obtained from these small children were not large, making accurate estimations difficult. The results obtained have been corrected for a 24-hour period. In Case 1 only traces were found, but in Case 3, it is interesting to note that nearly six times as much 5-HIAA was found after the injection of codeine. It is not possible to attribute any particular significance to this solitary estimation. The other results are in agreement with the essentially normal values reported by Rider and Davis in cases of generalized urticaria pigmentosa associated with cutaneous flushing.

Cutaneous flushing presents one more facet in the expanding picture of urticaria pigmentosa. It may be caused by histamine, or 5-HT, or, very possibly, by both. The ability to produce it by mechanical and chemical stimulation opens a new avenue to the investigation of the biochemical background of this complex disease and offers a new approach to the physiological behavior of the mast cells.

Summary

Three cases of generalized flushing of the skin associated with urticaria pigmentosa are recorded. In two, the flushing was induced mechanically by rubbing solitary nodular lesions of urticaria pigmentosa; the third child had generalized urticaria pigmentosa, and the flushing was induced by the injection of codeine phosphate. The relationship of the flushing of urticaria pigmentosa to the flush of the carcinoid syndrome is discussed.

429 Medical Arts Building (1).

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Familial Benign Chronic Pemphigus

The Role of Pyogenic Bacteria

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The belief that cutaneous infection with pyogens plays an important part in the genesis of lesions of familial benign chronic pemphigus (FBCP) arose from a few chance observations and has been strengthened by experimental evidence. I propose beginning with an account of the steps by which this conclusion was reached and leaving a discussion of the previous literature to a later part of this paper.

Report of Cases

CASE 1.—A white woman, age 56, was first seen on July 27, 1951. Since the age of 17 recurrent vesicular and bullous lesions have affected the axillae and occasionally the sides of the neck. Attacks tended to occur in the late winter (i. e., July to September in South Africa) and to last for about six weeks. Intervals of freedom varied from a few months to several years. In the past, a few exposures to roentgen rays had always cleared the lesions. Her father (deceased) had a skin condition of the groin, unidentified, for many years. Clinical and histologic examination were typical of FBCP. Treatment with vitamin A and a local application of boric and starch powder was followed in five weeks by healing of all lesions. A relapse occurred about a month later, and the patient did not attend again. In February, 1952, her husband telephoned to say that the lesions had cleared dramatically within a week of beginning to use a 3% chlortetracycline ointment. I spoke to the patient again in November, 1958, and was told that she has remained well except that the slightest scratch or abrasion may cause a blister to appear; this responds rapidly to the application of any antibiotic ointment.

Comment.—In 1952, I attached no importance to the news that chlortetracycline ointment was effective. The unpredictable succession of recoveries and relapses reported in cases of this disease, together with the known tendency for patients to recover completely with advancing years, seemed at that time to be a sufficient explanation of her recovery.

CASE 2.—A white man, age 44, was first seen Dec. 23, 1954. He stated that "eczema" had begun in 1941, affecting mainly the shoulders, neck, and popliteal areas; attacks had also involved other areas, including groin and scrotum. Itching was pronounced, and the attacks occurred more frequently and with greater severity in summer. From 1949 to 1952, there had been complete freedom. Local applications of penicillin had at first been highly successful but had gradually lost their effect. A few injections of corticotropin had not helped. His father and two brothers had a similar "eczema," the former chiefly on the neck.

Physical examination showed only lichenified areas behind the knees. White dermographia was not elicited, and intradermal testing with 25 randomly selected allergens showed five doubtful positive reactions. A simultaneous paired comparative trial of 1% hydrocortisone ointment and 1% hydrocortisone plus 0.5% neomycin ointment was made; the addition of neomycin was seen to cause almost complete healing of lesions, which were practically uninfluenced by hydrocortisone alone. No diagnosis was made, and the patient was not seen for three years. On Nov. 29, 1957, the patient reported with a fresh, florid attack of nummular lesions. These showed central clearing and a rapidly advancing vesiculopustular edge (Fig. 1). The patient stated that these lesions had begun at the sites of sunburn papules which he had scratched. A biopsy specimen from the spreading edge of the lesion illustrated (Fig. 1) showed the features of FBCP (Fig. 2). Direct and cultural examination from blister tops at the edge of a lesion showed no fungi. While awaiting the result of the biopsy, I prescribed 3% tetracycline ointment to be applied to two of his three lesions. One week later these had healed and the third, untreated, lesion had become larger. This also cleared in a few days with the application of tetracycline ointment. His subsequent history has been obtained by correspondence: Tetracycline gradually lost its efficacy and other

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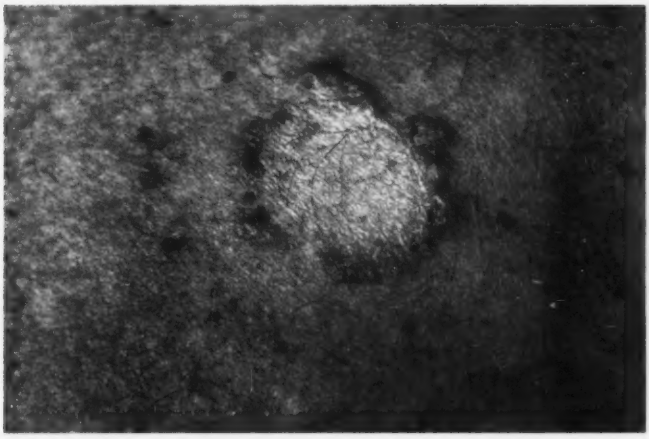

Fig. 1 (Case 2).—Recent lesion with advancing edge. Note resemblance to a microbial infection.

antibiotic ointments are now used at random, usually with prompt healing.

Comment.—This case presented lesions which clinically resembled an acute, superficial pyoderma, as well as older lesions which resembled atopic dermatitis. It will be recalled that Case 4 in the series of Lyles, Knox, and Richardson[1] had been regarded as one of neurodermatitis disseminata. Of particular interest is the dramatic initial success of locally applied penicillin, neomycin, and tetracycline in turn, each of these antibiotics gradually losing its effect. At this stage it occurred to me to refer to my notes on Case 1, whose response to topical chlortetracycline now seemed suggestive.

CASE 3.—A white woman, age 46, showed no previous skin trouble in her personal and family history. Three weeks previously two itching papules had appeared on the back and left side of the neck; each had been scratched and had become enlarged. Examination showed two roughly circular areas, 3 and 5 cm. in diameter, with clearing centers and peripheral flaccid bullae. A biopsy specimen (Fig. 3) was consistent with the diagnosis of FBCP. Again 3% tetracycline ointment was prescribed, and the patient was asked to present herself at a meeting of the Transvaal Dermatological Society three weeks later. By this time, healing had taken place and the sites of the previous lesions were difficult to locate. Since then, two summer attacks have occurred; the first cleared in a few days with tetracycline ointment. Seen at the beginning of the next attack, a culture was made from an unruptured vesicle; this showed a nonhemolytic Staphylococcus pyogenes var. aureus and

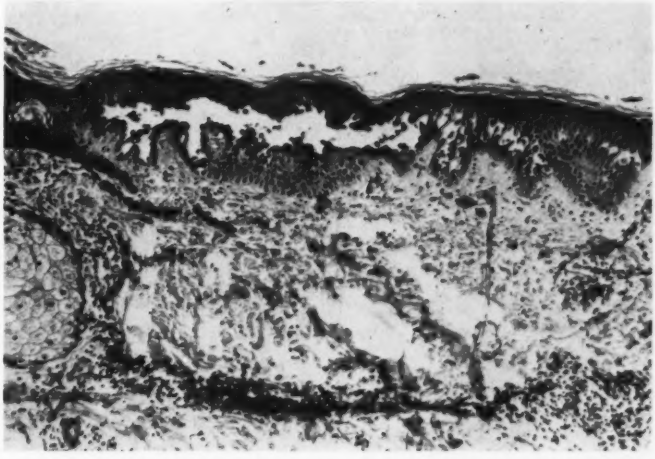

Fig. 2.—Histologic appearance from edge of lesion seen in Figure 1. Reduced 30% from mag. × 120.

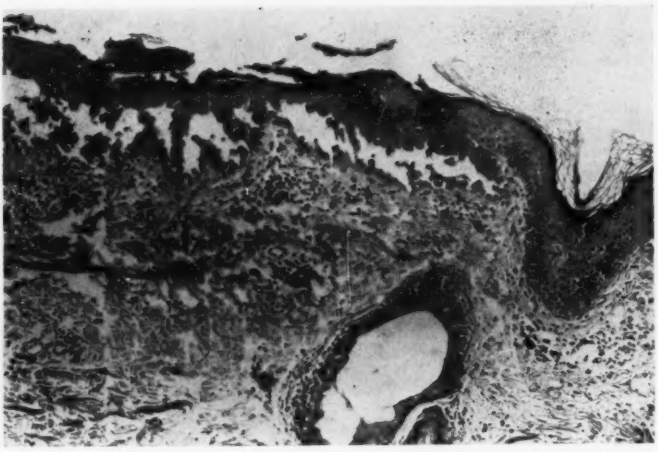

Fig. 3 (Case 3).—Biopsy specimen. Reduced 30% from mag. × 120.

Fig. 4 (Case 4).—Biopsy specimen. Overlying the vesicle on the right is a seropurulent crust. Suprabasal acantholytic clefts are seen below; × 120.

an unidentified Gram-positive coccus. The sensitivity tests showed both organisms sensitive to a variety of antibiotics, including tetracycline (100μg. per milliliter), but the Gram-positive coccus was insensitive to erythromycin. Meanwhile, a 3% erythromycin ointment had been prescribed and found to be ineffective, the lesion becoming steadily larger; changing to tetracycline ointment resulted in complete healing in five days.

Comment.—The selective response to an antibiotic effective in vitro, and lack of response to another which was found inert in vitro against one of the organisms isolated, are noteworthy.

CASE 4.—A white woman, age 24, was first seen on Oct. 24, 1958. "Sores" had been present on the back of the neck and in the axillae for six months; they gave rise to a burning itch. Numerous applications, including locally applied hydrocortisone, had not helped. The lesions were irregular crusted plaques with flaccid bullae at the circumference. Clinically and histologically (Fig. 4) the condition was typical of FBCP. Her father (Case 5) had had a similar condition beginning at the age of 30, recurring in late winter, and not present for the last five years. After three days of 3% tetracycline ointment the lesions were estimated to be 70% clear, and complete healing was obtained in three weeks. A few areas on the neck, however, still showed a hyperkeratotic, verrucose appearance, which vanished after a week's application of 3% erythromycin ointment, leaving faint pigmentation.

Comment.—This case appeared to confirm the hypothesis founded on the previous three, that efficient topical antibiotic treatment could produce healing of the lesions. I, therefore, obtained the patient's permission to conduct the experiment described in the next section.

Experimental Evidence

If pyogenic infection in a predisposed subject produces the clinical and histologic features of FBCP, then these should be capable of deliberate reproduction. I, therefore, used laboratory cultures of coagulase-positive S. pyogenes var. aureus as follows:

An area about 2 cm. in diameter was selected over each scapula; no previous lesions had appeared at these sites. The areas were cleaned with alcohol and then lightly abraded with sandpaper, so lightly that only the slightest roughening could be seen with the loupe and no loss of tissue was visible. A culture of Staphylococcus was rubbed into one of these areas with a sterile spatula, then it and the control (abraded but not inoculated) area were covered with sterile nonmedicated gauze and adhesive tape. Punch biopsies were taken from both areas after 72 to 96 hours and histologic preparations made.

The results were as follows: 1. Case 4 was seen after 72 hours. The control site was indistinguishable from normal skin, both on inspection and by histologic examination. The inoculated site, however, showed an area of erythema with several barely visible flaccid bullae and a few crusts (Fig. 5); it resembled closely some of the smaller lesions which had appeared spontaneously on the neck and in the axillae. A 5 mm. punch biopsy specimen showed features typical of FBCP (Figs. 6 and 7);

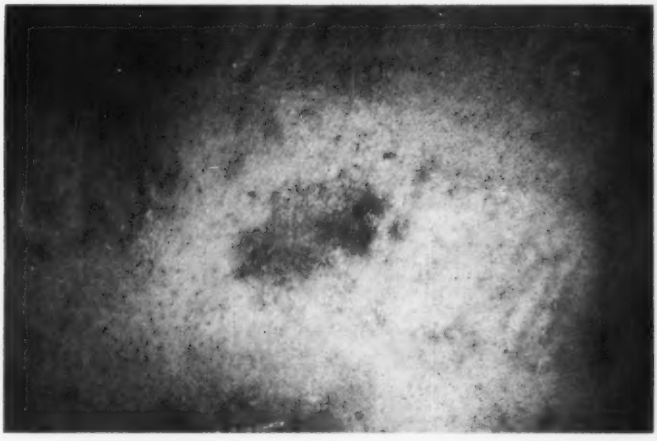

Fig. 5 (Case 4).—Appearance 72 hours after surface application of Staphylococcus culture. Note spread to the right.

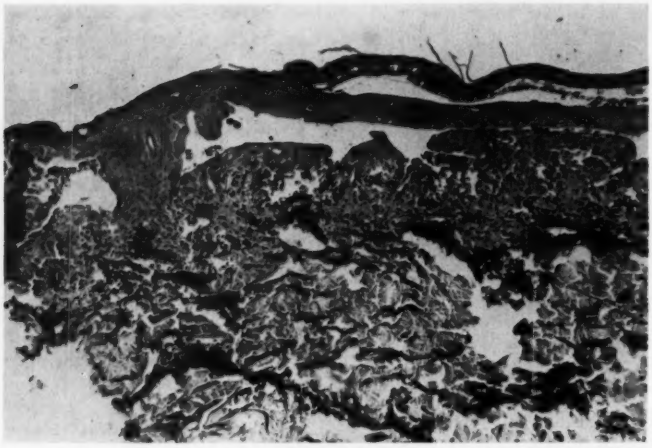

Fig. 6 (Case 4).—Biopsy specimen from artificially produced lesion (see Fig. 5). Reduced 30% from mag. × 120.

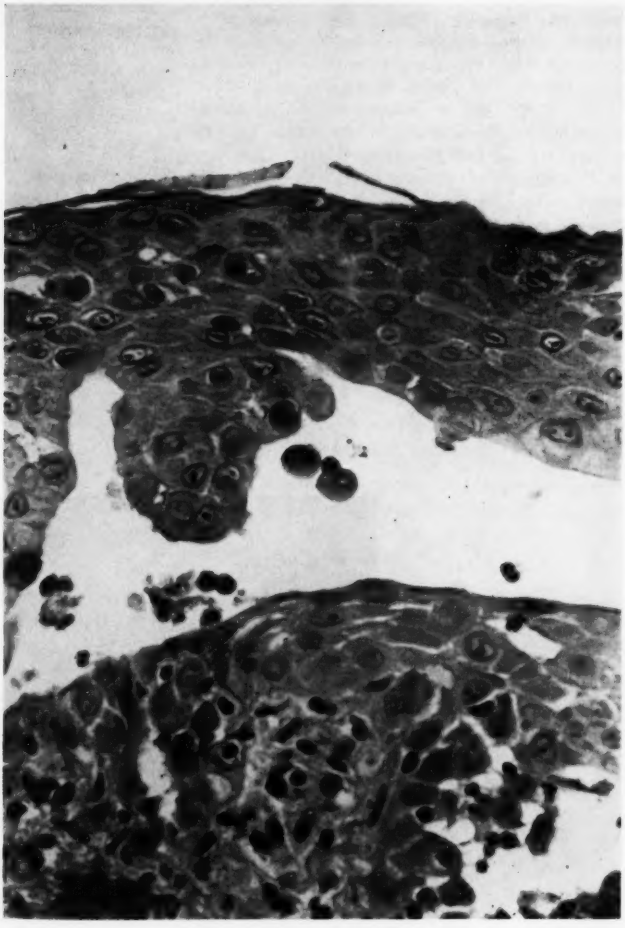

Fig. 7.—A part of Figure 6. Note acantholytic cells; × 480.

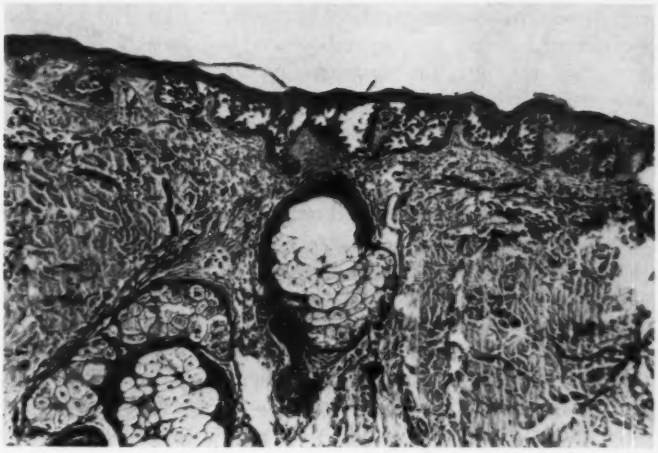

Fig. 8 (Case 5).—Biopsy specimen 96 hours after surface application of Staphylococcus culture. Reduced 30% from mag. × 120.

it will be noted that, in addition to the vertical clefts shown in this photomicrograph, there are several larger horizontal ones. Examination of various levels showed that none of these horizontal clefts were subcorneal and supragranular, i. e., in the area affected by impetigo contagiosa. There is a marked resemblance between this artificially-produced lesion, as pictured here, and the photomicrograph of a spontaneous lesion in the article by Pinkus and Epstein.[2]

2. Case 3 showed no visible difference from normal skin in either the inoculated or control areas, and biopsies were not performed.

3. Case 5 (father of Case 4). This subject, age 62, had shown no spontaneous lesions for five years. Seen 96 hours after light abrasion and rubbing in of a culture of Staphylococcus, the control area was normal and a biopsy specimen from it showed normal histologic features. The inoculated site showed a hardly perceptible erythema and several flaccid bullae, best seen when the skin was stretched or twisted by the examiner's fingers. A biopsy specimen from this area showed the characteristic features of FBCP (Figs. 8 and 9). It should be noted that in this subject, who had presumably reached the stage of spontaneous recov-

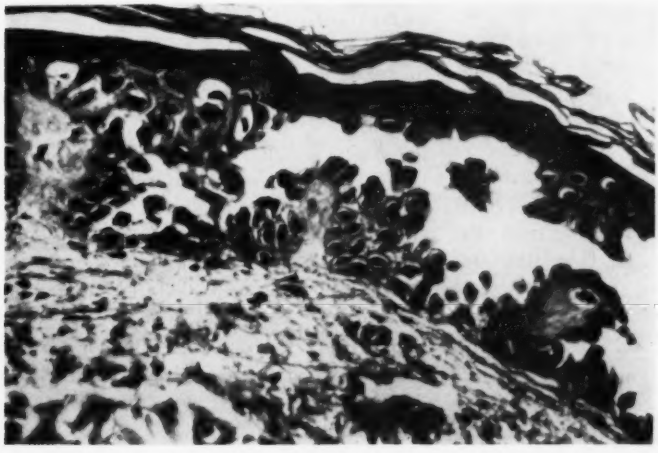

Fig. 9 (Case 5).—Note villi and various forms of acantholytic cell. Reduced 30% from mag. × 480.

ery, as seen in an elderly patient by Coles,[3] the clinical features were not reproduced in a typical form, though the histologic appearance was characteristic.

In assessing these two successful attempts at reproducing manifestations of the disease, the role of trauma must not be overlooked. Haber and Russell,[4] as well as Forman and Calnan,[5] produced erythema and hemorrhagic puncta by friction with gauze; these areas then showed the typical acantholytic clefts on immediate histologic examination. In my own subjects friction was so light that no erythema was produced, and biopsy specimens from the lightly abraded control sites showed no deviation from the normal. Furthermore, the lesion produced in Case 4 was a spreading one and had extended under the gauze pad and outside the abraded site to abut on one of the areas of application of adhesive tape (Fig. 5). The lesion, in other words, was growing eccentrically and had invaded nonabraded skin.

Comment

It is generally agreed that FBCP is an inborn abnormality of the skin, transmission showing itself as an irregular dominant.[6] It is noteworthy that all available reports from the English language literature, as well as my own cases, mention the onset of the condition after puberty, sometimes in middle age. On this score alone Gougerot's [7] claim to priority must be suspected, for the proband in Gougerot and Allée's article [8] was aged 4 years and had shown a succession of bullae since birth, as had his relatives. Moreover, the bullae in Gougerot's family were of short duration but frequent recurrence, an observation quite at variance with the type of lesion and its evolution described by others, and Degos [9] is not satisfied that the diseases described by Gougerot and Allée,[8] on the one hand, and Hailey and Hailey,[10] on the other, are nosologically identical.

The identity of FBCP and Darier's keratosis follicularis has been the subject of controversy since it was first claimed by Ellis,[11] and conflicting opinions are encountered.[12] I do not propose contributing to this controversy, beyond remarking that none of the histologic preparations studied in the course of this investigation showed any suggestion of Darier's disease, apart from the suprabasal clefts which are common to the two conditions.

All are agreed that FBCP is a genodermatosis: it now remains to determine what are the precipitating factors in the production of lesions. In their original article Hailey and Hailey [10] stated, "Possible etiologic factors, such as occupational effect, ingestion of drugs, exposure to sunlight, irritation from clothing or from chemicals and presence of an anatomic anomaly, have been definitely eliminated. . . ." With the exception of traumatized areas showing excessive fragility of the epidermis in a suprabasal position,[4,5] no previous experimental work seems to have been done.

Investigations and suggestions regarding the secondary role of bacteria may be briefly summarized. Ayres and Anderson,[13] in their independent discovery of the disease under the title of "Recurrent Herpetiform Dermatitis Repens," made cultures from unruptured bullae and, with two exceptions, isolated staphylococci or streptococci. They also, as the word "repens" implies, drew attention to the spreading nature of the lesions, a sign which is at least suggestive of microbial activity; they did not, however, hazard a guess regarding the etiologic role of bacteria. The similarity of the lesions to banal impetigo is mentioned by several authors,[6,10,14] and Herzberg [6] mentions the speed with which the clear vesicular contents become turbid and seropurulent. Norrlind and Blumenthal [15] cultured staphylococci repeatedly from the bullae in their case and suggested their etiologic significance. Foerster [16] even went so far as to call the condition a "pemphigoid pyoderma," rather than FBCP; he considered the condition to be of streptococcic origin and stated that it eventually responded to treatment along those lines.

Mali and Zoon [14] point clearly to the reason why the majority of authors have ignored the role of pyogenic bacteria in FBCP: "From the clinical aspect, the affection very much resembles . . . the impetigo vulgaris (circinata). The exceptional obstinacy and the hereditary feature of the affection excludes this diagnosis."

Response to antibacterial treatment as a clue to etiology must not be given undue importance, especially when dealing with a disease whose fluctuations are often unpredictable. Nevertheless, systemic therapy with penicillin [17] and chlortetracycline [18,19] have had their advocates, and Lyles, Knox, and Richardson [1] claimed beneficial results from various systemically given antibiotics. As there is no record of such antibiotics being selected according to the sensitivities of the bacteria concerned, one could not expect them to be effective in every case; in vitro, at all events, Lewin and Loewenthal [20] showed that an antibiotic selected at random for systemic use would be effective against less than half of cutaneous pyogenic bacteria. A few reports also mention the beneficial effect of sulfonamides,[2,14,15,21] the occasional swelling of regional lymph nodes,[2] and the finding of polymorphonuclear leukocytes in the affected skin are in keeping with the concept of a bacterial infection.

Though the acantholytic cell is often regarded as specific for pemphigus and FBCP, we must remember that acantholysis can occur in other conditions. The balloon cells of certain viral dermatoses show acantholytic changes, and they have repeatedly been demonstrated in various forms of pyoderma. Thus, Steigleder [22] pictures typical "pemphigus cells" found in smears from a case of recurrent pyoderma of the anal and genitocrural regions.* Unna's description of impetigo streptogenes [23] notes free-floating "balls of epithelial cells" in the vesicle and that "the papillary body is swollen, and, partly covered with prickle layer, projects naked into the pustule." McCarthy [24] states that in impetigo circinata "the floor of the vesicle is made of loosely attached, degenerated rete cells similar to those seen in herpes zoster. . . . Unna believes that the cells of the rete are loosened up and destroyed by the so-called balloon type of degeneration. . . ." This is confirmed by Gans and Steigleder,[25] *who also stress the extraordinary difficulty of differentiating pemphigus and circinate impetigo histologically in certain cases.*[26] In Bockhart's impetigo, too, the same authors mention the presence of balloon cells in the pustule, a finding which I have confirmed in my own material, where these "balloon cells" are seen to be indistinguishable from the acantholytic cells of pemphigus. Similar cells have been seen and pictured in subcorneal pustular dermatosis [27] and in spontaneous symmetric eczema,[28] as well as in blisters caused by cantharidin and croton oil.

* Although Steigleder stated that FBCP could be excluded in this case, he does not say on what grounds.

Conclusions

The facts so far recounted have led me to the conclusion that FBCP is a manifestation of pyoderma (impetigo circinata) in persons with an inherited predisposition to acantholysis. The frequent localization of lesions to the back and sides of the neck, the axillae, and the groin could be explained by the excessive friction and/or maceration which may occur in these areas; this hypothesis would also explain the usual exacerbations in hot weather, when flexural impetigo (pyosis Mansoni of the tropics) is more likely to occur. Even the gradual improvement with advancing years could be attributed to an increasing immunity to pyogenic bacteria; the possibility of deliberately producing lesions even in these circumstances, as in Case 5, is to be noted.

Summary

Familial benign chronic pemphigus (FBCP) has been found to resemble impetigo circinata in the following respects:

(*a*) Clinical appearances, as noted by many authors.

(*b*) Fresh lesions were produced in two out of three trials by surface inoculation of Staphylococcus pyogenes var. aureus. The histologic appearance of these artificially produced lesions was identical with that of spontaneous lesions in FBCP.

(*c*) Response to topical antibiotic therapy.

Attention is drawn to the presence of acantholytic cells in conditions other than pemphigus, notably in impetigo circinata.

It is suggested that FBCP is an inherited abnormality, which shows itself by an exaggerated tendency to produce epidermal fission by acantholysis, especially as a response to pyogenic infection.

Dr. S. Holman supplied the cultures used in the experimental work and reported on the in vitro sensitivities of bacteria from Case 3. Photomicrographs are by M. Ulrich of the S. African Institute for Medical Research.

Department of Medicine, General Hospital.

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The Present Status of Military Dermatology

COL. ROBERT S. HIGDON (MC), U. S. Army

This review will encompass the dermatologic activities of the U. S. Army, Navy, Air Force, and Public Health Service from 1946 to the present time.

The high standards of medical care available today throughout the Armed Forces and Public Health Service have evolved from a vast post-World War II training program of Regular medical officers in the various specialties of medicine. As a result of this program, present-day specialized medical care in major installations of the Armed Forces and Public Health Service is comparable to the highest standards found in civilian medical practice.

The most important mission of Federal dermatologists is to furnish the best possible care to the large number of active and retired duty personnel and their civilian dependents. Some of the additional responsibilities include the training of specialists in dermatology and venereal diseases and giving consultative service to the respective Surgeons General regarding standardization of drugs and equipment, new methods of therapy, revision of regulations and directives pertaining to the specialty of dermatology, and similar related matters.

Historical Background

Inasmuch as I am personally more familiar with the beginning dermatologic training activities in the Army, I shall limit my comments chiefly to this branch of the services.

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Presented at the American Academy of Dermatology and Syphilology, Chicago, Dec. 10, 1958, on the Round Table Panel of Military Dermatology.

Consultant in Dermatology to The Surgeon General, U. S. Army; Chief of Dermatology Service, Walter Reed Army Hospital, Washington 12, D. C.

Prior to World War II, there were no trained dermatologists in the Army and patients with skin disorders were customarily treated by urologists, some of whom became very proficient in the diagnosis and treatment of the commoner dermatoses.

During World War II, many expert dermatologists from civilian life served in all branches of the Armed Forces. Upon cessation of hostilities, almost all of these specialists returned to their private practices during the years 1945 and 1946. The many important contributions which they had made while still in military life, however, not only won them much praise but also convinced the military medical authorities that dermatology should be continued as a specialty in the postwar Federal services.

The problem of how to train Regular Army medical officers to replace the departing highly trained Reserve Corps dermatologists was a considerable one at first, because no Army hospitals were equipped or approved for training in this specialty. By January, 1946, the Army Surgeon General's Office had received applications from three Regular Army medical officers to take training in dermatology, and these officers were sent to Ashford General Hospital, White Sulphur Springs, W. Va., where, under the supervision of Lieut. Col. Herbert L. Traenkle and his assistant, Capt. Leslie Nicholas, the first attempt was made to establish a dermatology training program. Both of these Reserve officers were diplomates of the American Board of Dermatology. The closing of this hospital four months later, however, necessitated discontinuation of the program, and the three trainees were transferred to widely separated stations, where it could only be hoped they might find individual opportunities for

further training. The impressive Army Professional Training Program, which was destined to become such a success in future years, was still only in the planning stage in 1946. Consequently, the early would-be "residents" had to shift for themselves and take advantage of any and every opportunity that presented itself to improve their knowledge in the specialty of their choice.

The fledgling Army dermatologists did indeed take advantage of every opportunity and with the helpful cooperation of civilian training centers and the full support of The Surgeon General each of the upcoming Regular Army dermatologists received at least one year of formal training in civilian institutions. The remainder of their training was done by their boot straps. In 1947, however, three Army hospitals (Walter Reed, Brooke, and Letterman) were approved for two years of formal training by the American Board of Dermatology, and during the next few years most Army residents took two years of training in Army hospitals and one year in a civilian institution. Eventually, all three Army hospitals mentioned above were approved for the full three years of residency training, and now all Army residents receive their entire training in Army hospitals.

The post-World War II preparation for the training of dermatology residents in the Navy, Air Force, and Public Health Service was essentially the same as that of the Army. All of the services started their training programs without the benefit of any antecedent dermatologic organization or foundation.

Present Training Facilities

Army.—Residents in this branch of the service are given all of their training in Army hospitals. This also applies to Air Force residents who are trained in Army hospitals. The following hospitals are approved by the American Board of Dermatology:

1. Walter Reed Army Hospital, Washington, D. C., presently has a total of 12 residents. Included in this total are three Air Force residents, since the Air Force customarily sends one resident to this hospital to begin his training in July of each year.

2. Brooke Army Hospital, San Antonio, Texas, has a total of nine residents. Col. George Prazak is the Chief of Dermatology Service.

3. Letterman Army Hospital, San Francisco, has a total of four residents. Col. Raymond M. Williams is the Chief of Dermatology Service.

The total resident capacity of these three Army hospitals is 25, which is the number presently assigned. Competition for these residency appointments is very keen.

Although these Army hospitals are approved for three years of training, the Army does not have so many diplomates available for teaching that it can call itself independent. As a matter of fact, the training programs in all three of these hospitals would no doubt have been discontinued long ago if it were not for the continued, competent, and faithful services of our civilian dermatology consultants. Most of them are on the staffs of university medical schools in their respective cities, and the expert assistance they have given us as consultants for the past 12 years is incalculable.

Navy.—Residents in this branch of the service take either two years of training in Naval hospitals and a third year in a civilian hospital or all three years of training in a civilian hospital.

The following Naval hospitals are approved by the American Board of Dermatology:

1. U. S. Naval Hospital, Philadelphia, Pa. Capt. James H. Lockwood is the Chief of Dermatology Service and presently has three residents. Three additional residents from this hospital are now at the Graduate School of Medicine of the University of Pennsylvania, where they customarily take one of their three years of training.

2. U. S. Naval Hospital, San Diego, Calif. Capt. William N. New is the Chief of Dermatology Service and has five residents. Usually, residents take two years of training at this hospital and their third year at the University of Southern California.

Four additional Navy residents are taking their entire three-year period of training at New York University.

Air Force.—The Air Force does not have a hospital approved for dermatology resi-

TABLE 1.—*Military and U. S. P. H. S. Dermatologists Trained from 1946 Through 1958*

Army	Navy	Air Force	U. S. P. H. S.
24 Army trained	35 Navy & civilian trained	3 Army trained	10 U. S. P. H. S. & civilian trained
13 Army & civilian trained	8 Civilian trained	6 Army & civilian trained	11 Civilian trained
2 Civilian trained		4 Civilian trained	
—	—	—	—
39 (48 If Air Force included)	43	13	21

dency training. At present, there are three Air Force residents in training at Walter Reed Army Hospital and four residents taking their training in separate civilian institutions.

Training Accomplishments

Tables 1 through 4 summarize the accomplishments made as a result of the training programs carried out by the Federal services from 1946 through 1958.

TABLE 2.—*Data on Board Examinations*

	Army	Navy	Air Force	U. S. P. H. S.
Military & U. S. P. H. S. physicians who have taken board examinations	37	34	13	18
Military & U. S. P. H. S. physicians who have passed board examinations	35	33	12	17
% of success in board examinations	95 (35 out of 37)	97 (33 out of 34)	92 (12 out of 13)	94 (17 out of 18)

Public Health Service.—Residents in this branch of the Federal service are presently taking two years of training at the Board-approved U. S. P. H. S. Hospital in Staten Island, N. Y., and their third year in a civilian institution. Dr. Benjamin J. Chester is the Chief of Dermatology Service and has three residents. A fourth U. S. P. H. S. resident is now at Columbia University.

Service Problems

Until recently, the chief problem in all of the services, from a dermatologic viewpoint, has been the high attrition rate of service-trained Board diplomates. This has been particularly true of the younger age group, many of whom resigned as soon as their three-year period of "pay back time" had elapsed. In view of the recent enactment of

TABLE 3.—*Diplomates*

	Army	Navy	Air Force	U. S. P. H. S.
Losses	16 out of 35 (46%)	7 out of 33 (21%)	3 out of 12 (25%)	9 out of 17 (53%)
Presently on active duty *	19	26	9	8

* Diplomates trained prior to 1946 not included.

TABLE 4.—*Present Number in Training*

Army	Navy	Air Force	U. S. P. H. S.
22 Army hospitals	8 Naval hospitals	3 Walter Reed Army Hospital	3 U. S. P. H. S. Hospital, Staten Island, N. Y.
0 Civilian hospitals	7 Civilian hospitals	4 Civilian hospitals	1 Columbia University
—	—	—	—
22 (25 if Air Force included)	15	7	4

favorable legislation to make service careers more attractive, especially from a financial standpoint, it is hoped that resignations of young physicians will no longer constitute such a major problem. Anticipated retirements among the older age group, however, will make the continuance of our training programs mandatory.

I cannot speak for the other services, but in the Army we have never reached the point during peace time where there has been a sufficient number of dermatologists available to provide world-wide coverage for each of our major medical installations.

I have personally visited every Army dermatology clinic in the Far East and Europe and many in the United States and can assure you that each of our dermatologists is a very busy person and usually sees 600 to 1,000 outpatients each month. There are a few stations, however, where outpatient loads for a single dermatologist may reach a total of 1,200 to 1,500 a month. It is one of our goals to assign an additional dermatologist to each of these extremely busy hospitals as soon as possible.

The professional problems encountered in the services are essentially the same as those in civilian practice. Contrary to the opinion held by many of my civilian confreres, the majority of patients seen in a military dermatology clinic is not limited to young males. Usually, just as many females are seen. In most areas, the civilian dependent population, which ranges widely in age, is equal to the military population. In areas where a large number of retired personnel reside, the geriatric aspect of dermatologic care becomes of major proportion.

The military dermatologist must be adaptable. He must be prepared to handle problems peculiar to extremes of climate and geographic location.

One difference between military and civilian outpatient practice is in the necessity of hospitalizing certain military personnel who live in barracks and consequently do not have the facilities to carry out treatment instructions as adequately as if they lived in their own homes. The hospitalization of these patients, however, adds only a small percentage to our inpatient hospital load.

Some problems in the military services are shared professionally, but not administratively, by our civilian colleagues. For many years, regulations have prohibited acceptance into the military services of persons who show evidence or give histories of having a persistent dermatitis. Nevertheless, each year a number of potential dermatologic cripples find their way into the services. A good percentage of these persons have atopic dermatitis, which may be temporarily quiescent at the time they are examined at induction centers. As a group, these atopic patients show a marked tendency to have severe exacerbations of their dermatitis under stress conditions. In military life, the inductee has little or no control over his environment. He cannot choose his food. He cannot choose his clothing. He cannot choose his climate. He cannot always dodge unpleasant work assignments. Attempts to retain these persons on active duty usually result only in their being frequently hospitalized, ineffectual in their duty assignments, and they constitute a waste of the taxpayers' money. We, therefore, attempt to ferret them out as soon as possible and administratively separate them from the service. Such separations are nonservice connected and noncompensable.

Research Activities

In consonance with the over-all development of our specialty in the Armed Forces, dermatologically oriented research programs on a full-time basis have been initiated by the services. The problems under investigation cover a wide spectrum of the basic sciences, including mycology, biochemistry, physiology, and pathology. In addition, the Armed Forces and Public Health Service support, by grants, a considerable proportion of dermatologic research being carried on by civilian institutions.

As part of a well-rounded training program, residents in dermatology are en-

couraged to participate in investigative work in either basic science or clinical spheres.

Recent Administrative Accomplishments

The Joint Armed Forces booklet, "Basic Diagnostic Nomenclature," which has been the source of considerable unfavorable comment by dermatologists, will be replaced with a new manual prepared by a Department of Defense Subcommittee on Diagnostic Nomenclature. Dermatologists and other specialists from all of the services will collaborate on the final product. Basically, the new manual will follow the International Classification of Diseases.

A new Technical Bulletin, Medical 230, "Treatment and Management of Venereal Disease," is being prepared by the Departments of the Army and the Air Force.

Army regulations regarding dermatologic standards of medical fitness for procurement and retention of officer and enlisted personnel are in the process of being completely revised.

All of the above cited publications are expected to be completed and distributed within the coming year.

Comment

I have outlined, in brief form, the growth and development of our specialty in the Federal services. I might add that we are very proud of its present status. It would be most neglectful, however, if the important role played by our civilian consultants were not emphasized. Their guidance and splendid spirit of cooperation have contributed immeasurably to the progress which has been made. We hope for continued assistance and encouragement in our attempt to provide the best of dermatologic care to all those for whom we are responsible, both at home and abroad.

Summary

Dermatologic activities in the U. S. Army, Navy, Air Force, and Public Health Service from 1946 through 1958 are presented.

Acknowledgment is made to the following officers for their assistance in the preparation of statistical data: Col. George Prazak (MC), Col. Raymond M. Williams (MC), and Major Michael J. Davis (MC), U. S. Army; Capt. John W. Albrittain (MC), Capt. James H. Lockwood (MC), and Capt. William N. New (MC), U. S. Navy; Col. Robert E. Lyons (MC) and Major James M. Kennedy (MSC), U. S. A. F.; Benjamin J. Chester, M.D., and Eugene J. Van Scott, M.D., U. S. Public Health Service.

A View of Keratosis Follicularis (Darier's Disease) as a Neoplastic Process

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For the past eight years we have had under our care a remarkable treatment-resistant progressive case of Darier's disease. We should like at this time to summarize certain findings in this patient. Despite the fact that many of these studies are largely of a negative type, they are presented in the hope that they will stimulate further research in this challenging and baffling disease.

Report of a Case

CASE 1.—This patient, now 18 years old, was first seen as a boy of 10 years. A scaling pruritic plaque had first appeared on his scalp at the age of 9 years. This rapidly extended over the entire scalp and on to the forehead. At the time of his initial visit he presented the classic keratotic lesion of Darier's disease (Fig. 2). His mother likewise showed skin lesions typical of Darier's disease, and, by history, her sister had the same affliction. Despite varied topical and systemic treatment, the eruption slowly and progressively extended to include most of the head, neck, and trunk (Figs. 1 and 3). The arms and legs have remained relatively exempt. The severity of the eruption is now such as to threaten normal social existence.

In the summer of 1958 the patient was hospitalized and numerous tests, both diagnostic and therapeutic, were conducted to learn more concerning this patient's problem. The salient features are outlined.

History

(1) Familial nature—mother and aunt.
(2) Process flared by sunlight, emotional stress, upper respiratory infections.
(3) Tinea capitis preceded eruption by one year.

Physical Examination.—Enormous plaques of fissured, hyperkeratotic, erythematous, malodorous dermatitis covered all of the seborrheic areas. At the periphery, numerous, discrete, yellow-brown, waxy, keratotic papules were found. The palms showed localized keratotic lesions. The nails showed dystrophic changes in the form of leuconychia, onycholysis, and striate thickenings of various nails of both the fingers and toes. Verrucae vulgares were present on the hands and digitate verrucae in the paranasal area.

The general physical examination was normal.

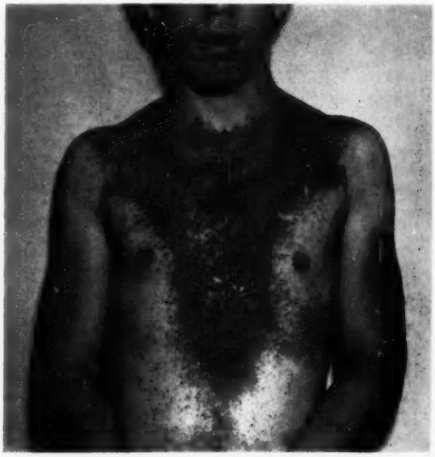
Laboratory Findings.—Blood cell count, urinalysis, blood sugar, BUN, and bleeding time were normal.

Total serum protein was 6.6 gm. (albumin 2.90, α_1-globulin 0.43, α_2-globulin 0.57, β-globulin 0.74, and γ-globulin 1.97). This protein spectrum is compatible with chronic secondary widespread cutaneous bacterial infection, inasmuch as the γ-globulin is elevated.

Bacterial culture revealed Staphylococcus pyogenes var. albus, Bacillus proteus, Escherichia coli, diphtheroids, and β-hemolytic streptococci. Chloramphenicol was effective in vitro against all of the organisms except the streptococci. The latter were shown to be sensitive to penicillin.

Biopsy.—Two biopsy specimens from selected sites showed changes typical of Darier's disease. Several verrucae were removed and found to have

Fig. 1.—View of seborrheic distribution pattern of lesions of keratosis follicularis in patient as seen in July, 1958.



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Department of Dermatology, University of Pennsylvania School of Medicine.

Fig. 2.—Appearance of lesions on back as seen in October, 1954.

typical cytology of a verruca, with numerous inclusion bodies. No changes were seen in the verrucae which would suggest Darier's disease.

Skin Tests.—Ultraviolet-light irradiation, 3 minutes, 15 in., three times daily (Hanovia hot quartz), to a normal skin site produced typical keratosis follicularis (Fig. 4), proven by histologic study (Fig. 5). These lesions persisted for six weeks, eventually fading completely.

Inunction of

Hydrous wool fat 1% in benzene Sebum pooled normal 1% in benzene Sebum (from patient's scalp, ether washing) 1% in benzene 3-4,benzopyrene 1% in benzene	None of these gave a local reaction despite local daily application to normal skin on right thigh for 2 months.

Grenz rays, 500 r, 12 ma., 15 kv. to lesion gave temporary involution.

Intradermal injections in lesions:

Chloroquine 1% Testosterone 5% Estrone 0.1% Progesterone 2.5% Triamcinolone 5% Dexamethasone 1% Hydrocortisone 5%	All without local therapeutic benefit.

Response to Treatment

Topical:

Steroid—creams, ointments, sprays—no help.
Antibiotic creams, lotions, powder—no help.
Vitamin A ointment—no effect.

Systemic:

Chloramphenicol * Novobiocin †	Helpful in reducing secondary infection, no effect on noninfected lesions.
Chloroquine # Amodiaquin *	Apparently helpful.

* Supplied by Dr. Leon Warren, Parke Davis & Company, Detroit.

† Supplied by Upjohn Co., Kalamazoo, Mich.

Supplied by Mr. J. R. Lucas, Winthrop Laboratories, New York, N. Y.

Fig. 3.—Appearance of lesions on back as seen in July, 1958. Note progressive nature of process over four-year period.

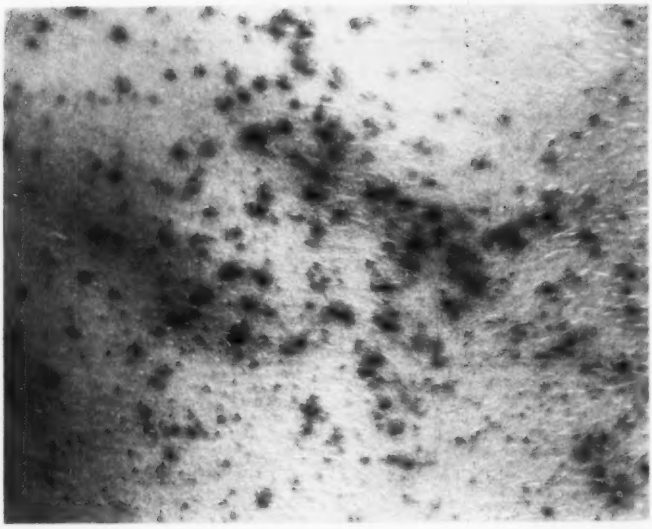

Fig. 4.—Close-up view of lesions of keratosis follicularis experimentally produced by exposure to ultraviolet light (hot quartz).

Ethinyl estradiol 0.05 mg. daily—no help.
Corticotropin, 40 units, ×2—no help.
Dexamethasone,‡ 6 mg. per day—no help.
Griseofulvin,§ 1 gm. per day, ×7—no effect.
Aminopterin,‖ 0.5 mg., ×14—no change.
Vitamin A, I. M., 100,000—no help.

Local Curettage and Electrodesiccation: Locally curative (Fig. 5).

‡ Supplied by Dr. Nicholas Capeci, Merck Sharp & Dohme, West Point, Pa.

§ Supplied by Dr. Gavin Hildick-Smith, Johnson & Johnson, New Brunswick, N. J.

‖ Supplied by Dr. Christopher Demos, Lederle Laboratories, Pearl River, N. Y.

Special Studies

Inoculation of fresh suspension of lesions into

Skin of normal human volunteers	No effect as observed over period of one month.
Irradiated with ultraviolet light	
Nonirradiated (25 subjects)	
Rabbit cornea (2 each)	
Rabbit ear	
Rat conjunctival sac (2 each)	
Skin, intradermal	
Skin, subcutaneous	
Intraperitoneal	
Hamster (2 each)	
Pouch	

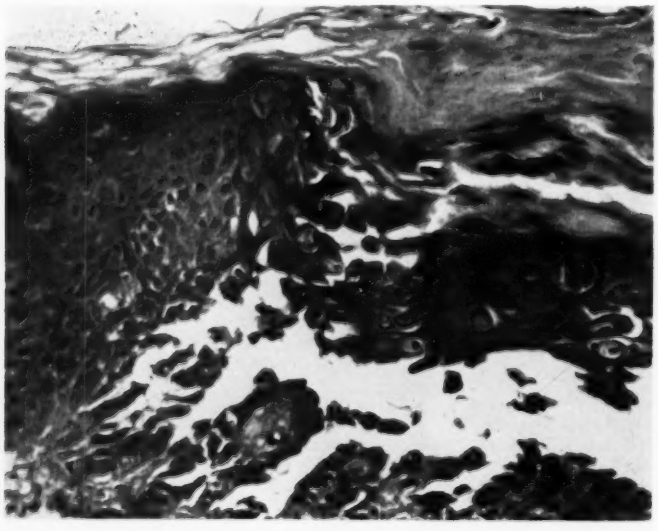

Fig. 5.—Histologic findings in experimentally produced keratosis follicularis. Reduced 15% from mag. × 300.

Comment

Throughout all of the writings on Darier's disease [1] courses the unifying theme that this is a familial, hereditary, genetic defect in the skin. The patient we have presented had a typical history in this regard. Both his mother and his aunt had typical lesions of Darier's disease. However, throughout all of our investigation the question constantly arose, in what way does the genetic factor operate? After considerable attrition of "beautiful theories by ugly facts," we were able to pose the following three seemingly significant questions:

A. Is Darier's disease an unusual Koebner reaction to seborrheic dermatitis?

The strict localization of our patient's eruption to the seborrheic areas and the appearance of the problem at or just prior to puberty strongly suggested that an underlying seborrheic dermatitis might be triggering an unusual hereditary reaction pattern. In an analogous way we see psoriasis triggered by seborrheic dermatitis. The seborrheic localization of Darier's disease is common, and it has long been found that the male or oily person is prone to a severer form of Darier's disease. As an example, Hambrick and Leedham reported 10 living cases in one family.[2] The average age of onset was at 10 years, and each of their patients had involvement of the scalp.

We could, however, reasonably rule out an underlying seborrheic dermatitis. The primary lesion in Darier's disease and in this patient is noninflammatory and epidermal. The use of systemic and topical steroids, so universally effective in combatting seborrheic dermatitis, was without effect. Moreover, dermatitis was not known to induce Darier's lesions in this patient.

B. Could Darier's disease be of viral origin?

In this event the hereditary feature might represent a deficient resistance or familial transfer. Certainly, this question is a popular one. Graham and Helwig [3] recently stressed the likelihood that single isolated lesions of Darier's disease may be viral. The cellular changes can be interpreted as viral inclusion bodies. Our conclusion in this area must be based on the negative evidence that we failed to find any transferable causal agent. We were unable to produce any pathologic changes in test sites in man and animals. The patient's brother and father presented no evidence of even abortive lesions of the disease. Interestingly, a known viral growth, the wart, grew normally in the skin soil of this patient. Finally, the lesions did not reseed in an island of skin which had been treated with curettage and electrodesiccation. Thus, our observations lend no direct support to the view that Darier's disease is of viral origin.

C. Is Darier's disease a neoplastic process?

With modern awareness of the role of viruses in neoplasia,[4] this third last question is closely related to the second, but in any event it proved for us to be the most significant. There is much in the nature and course of our patient's eruption to indicate that it actually is a benign local neoplasia related to sebum and sun. Furthermore, there is much to support the view that the hereditary defect is actually an increased susceptibility to the "carcinogenicity" of sebum and sunlight. To review our reasoning:

1. *Clinically*, the lesions of Darier's disease may be viewed as punctate keratotic neoplasms. By more than name, they are related to senile as well as seborrheic keratoses. Matching neither, they nevertheless are palpable proliferative growths. Hypertrophic versions with large tumors may occur, as detailed by Beerman.[5] Fortunately, the neoplasia is benign and not precancerous, since malignancy is a great rarity in Darier's disease.

2. The *histology* of Darier's disease reveals the dyskeratotic cell of neoplasia. Here is the same dyskeratotic cell which is seen in senile keratoses. Furthermore, not only do the cells have a neoplastic growth potential, but they also show a characteristic of early epidermal neoplasia, clearly de-

scribed by Sutton,[6] in his classic article. This characteristic is the lack of coherence of the epidermal cells. Such a lack of epidermal cohesiveness may account for the lacunae considered one of the pathognomonic signs of Darier's disease. The characteristic cell is therefore both dyskeratotic and acantholytic. Hyperplasia of the epidermis, sometimes labeled pseudoepitheliomatous, is a feature of the more active lesions.[5] Another feature common to experimental neoplasia and Darier's disease is the notable disturbance in the melanocyte.[5,7] Finally, the dyskeratotic cell, indeed structures resembling both the corps ronds and grains of Darier, may be seen early in experimental studies on cutaneous carcinogenesis.[7]

3. The lessons learned in *experimental carcinogenesis* [8,9] have remarkable relevance to the story of Darier's disease.

(*a*) In all studies on the experimental induction of tumors the *genetic pattern* is of prime importance. Resistant strains of mice may never show a response to repeated applications to the skin of even the most potent carcinogens. The analogy to Darier's familial hereditary patterning is evident.

(*b*) The first change in the skin in response to repeated carcinogen application is *hyperplasia* or a benign tumor. Malignancy is a distinct separate second stage. Here we would view Darier's disease as corresponding to the early benign neoplasia.

(*c*) Experimental carcinogens are legion in number but one group, the lipids,[10-12] are of remarkable pertinence to the problem under discussion. Thus, it has been shown experimentally that *cholesterol, as well as fatty acids, are carcinogenic.* Weakly carcinogenic, but still carcinogenic, these are the very substances poured out in the sebum [13] of these Darier patients. The distribution of the disease and the age of onset both point to sebum as a possible "carcinogen" active in inciting the neoplasia we see. In adolescence there is an enormous burst in the activity and size of the sebaceous glands. Indeed the very follicular and parafollicular localization of Darier lesions, as well as the slow insidious, seemingly surface spread (Figs. 3 and 4) of the lesions further supports the view that sebum is the inciting agent. Bear in mind that in experimental studies topical application of tars, for example, produces tumors which usually arise in the hair follicles.[14] We believe that sebum can be viewed as a key incitant of the lesions in our patient. It is true that our short-term experimental study failed to provide objective evidence for this, but we suspect that long-term application—months to years—is necessary as we view the slow emergence of the clinical lesions (Figs. 2 and 3). Our patient did not differ from other subjects studied with benzopyrene experimentally.[15,16] Very different was the rapid experimental response seen with ultraviolet light in our subject. One may question the role of sebum in lesions of Darier's disease in the mucous membranes.[17] Here, recurrent trauma may be the precipitating factor, as in leukoplakia.

(*d*) Students of experimental carcinogenesis have long been aware of a *cocarcinogenic* activity of certain substances or procedures. These cocarcinogens promote the action of such carcinogens as the lipids. Ultraviolet irradiation or sunlight is one of the best known and most effective [9] of the cocarcinogen group. The eliciting effect of both sunlight and ultraviolet light was repeatedly noted by both our patient and his mother. This is a rather common clinical finding. Our experimental induction of the lesions with ultraviolet light only served to confirm the early classic studies of Bettmann [18] and Preissman.[19] We view sunlight as a cocarcinogen that rapidly triggers the epidermal neoplasia. Sunlight is not a necessary factor, but its presence is almost invariably felt.

Other experimental cocarcinogens include croton oil and x-rays. Yet notable specificity is present, since mere injury with turpentine does not induce tumors. The list of cocarcinogens is matched in Bettmann's experimental study of Darier's disease by the fact that the cautery, as well as cantharidin plaster, could induce the classic lesions of

Darier's disease. It is interesting to note that these cocarcinogens probably act on the epidermis, rather than the sebum itself. Finally, another neoplastic process, the seborrheic keratosis, is well known for its tendency to arise on inflamed areas.

(*e*) The *anticarcinogens* add another strong analogy for the student of the comparative biology of experimental carcinogenesis [7] and Darier's disease. Heading the list of anticarcinogens found in experimental work on animals may be seen a substance of rather remarkable therapeutic activity in many cases of Darier's disease,[20] though not in Case 1. This substance is vitamin A! We suspect that vitamin A can have only a limited effect against the neoplasia-inducing activity of sebum (c. f. acne), and thus is not demonstrably effective in cases as severe as ours. Podophyllotoxin and dimercaprol (Bal) are other known anticarcinogens which thus might be tried in the therapy of Darier's disease. We suspect that chloroquine (Aralen),[21] a recent agent of some benefit in Darier's disease, could be considered as another anticarcinogen. Its mode of action is not entirely clear, but certainly it neutralizes some effects of ultraviolet light irradiation and definitely affects enzyme systems.

4. We would rest our case for the neoplastic nature of Darier's disease on a final group of *therapeutic observations.* Darier's disease responds best to the modalities which cure tumors. Surgical excision of the isolated lesion is curative. We found cogent evidence that curettage and electrodesiccation effectively eradicate Darier's disease even with hypertrophic lesions surrounding the entire square of treated skin. Grenz ray [22,23] has long been known to effect a local clearing of Darier's disease when given in cancerocidal dosage. Upton [24] has an interesting diagrammatic sketch of the effect of grenz ray in his paper on the radiobiology of the cancer cell. He reviews the modern concept that radiation effects its action by inhibiting deoxyribonucleic acid formation and thus has a genetic effect on the cell itself. The anticarcinogen effects of vitamin A and the antimalarials have already been discussed. Avoidance of sunlight is another therapeutic injunction given both to the patient with epitheliomas and to the patient with Darier's disease. One only need point out the signal failure of intensive systemic steroid dosage on Darier's disease and the neoplastic process in general.

Summary

On the basis of clinicoexperimental observations and a review of the literature, the view is advanced that Darier's disease (keratosis follicularis) is a benign abortive neoplastic process.

The key roles of genetics, sebum, and sunlight are interpreted in the light of concepts in experimental carcinogenesis.

Photographs by Edward F. Glifort Jr.

Duhring Laboratories, University Hospital, 36th & Spruce St. (4).

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CORRECTION

The following paragraph was omitted from the Special Report entitled "Meeting of the International Society for Human and Animal Mycology," written by Dr. Frederick Reiss and published in the July issue of the ARCHIVES, page 133/**95**.

The arrangement of the meeting of the International Society for Human and Animal Mycology was under the able leadership of the General Secretary, Professor R. Vanbreuseghem of the Institut de Medicine Tropical, Anvers, whose indefatigable efforts, devotion and congenial spirit made this meeting an unusual success.

Triquin (Triple Synthetic Antimalarial) in Dermatology

Response of Chronic Discoid Lupus Erythematosus, Light-Sensitivity Eruptions, and Miscellaneous Dermatoses

JAMES H. BENNETT, M.D., and REES B. REES, M.D., San Francisco

Triquin

The synthetic antimalarial drugs in recent years have proven to play an important role in the management of lupus erythematosus and light sensitivity eruptions. The use of these drugs was originally stimulated by Page's article on the use of quinacrine (Mepacrine) in the treatment of lupus erythematosus. Light-sensitivity eruptions were also successfully treated and recurrences prevented with quinacrine and chloroquine.[2,3] Leeper and Allende [4] compared the use of quinacrine, chloroquine, and amodiaquin, and indicated that the latter two were preferable. Plaquenil sulfate [5] was reported to be effective in these conditions with a lower incidence of side effects. Schoch,[6] in a recent article, reviews the use of the antimalarial drugs in these conditions and gives an extensive bibliography.

A physician is now faced with the problem of which of the antimalarial drugs to use in order to get a maximum response with the lowest toxicity. It cannot be predicted which patient will tolerate or respond to a given drug. Each antimalarial drug by itself may in certain instances prove superior to the others, either because the drug is better tolerated or because an optimum therapeutic response is obtained.

A combination tablet, Triquin, is under investigation. The tablet contains about one-fourth the usual maintenance dose of each of the constituents, quinacrine (Atabrine Hydrochloride) 25 mg., chloroquine (Aralen Phosphate) 65 mg., and hydroxychloroquine sulfate (Plaquenil Sulfate) 50 mg. Each component has been proven clinically for its efficiency in affecting the course of lupus erythematosus and light-sensitivity eruptions. The tablet offers a full therapeutic dose of antimalarials without depending upon a single agent. A single agent may not be tolerated in the amount required to produce a maximum clinical response. In addition, the antimalarials may act synergistically.[7]

The mode of action of the antimalarial drugs has not been completely explained. There apparently is an anti-inflammatory action in addition to a possible sun-screening effect. McChesney et al.[8] have shown that appreciable amounts of antimalarial drugs are deposited in the skin. The possibility that the antimalarials produce their beneficial effects by absorbing or screening offending rays is one theory of their action.[8,9] A broader spectral-absorption band is obtained by combining the antimalarials than if they are given alone.

Rein and Fleischmajer [10] reported on Triquin with excellent results in seven of ten cases with chronic discoid lupus erythematosus and three out of four cases of benign lymphocytic infiltration. They employed a high dosage schedule, starting with eight tablets daily. Three of the 14 patients developed temporary intolerable side-effects (diarrhea, vertigo, and muscle pains) on these dosages. The authors still felt there was a lower incidence of side-effects with Triquin as compared to Aralen or Plaquenil. They felt that side-reactions depended upon dosage and individual susceptibility.

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From the Division of Dermatology, Department of Medicine, University of California School of Medicine.

In another report,[11] of 34 patients with cutaneous lupus erythematosus treated with Triquin, 16 cleared, 17 improved, and one was considered a failure. The average dose was two to three tablets daily. The authors encountered one patient who developed an increased cephalin flocculation while on Triquin, and another patient developed an erythematous eruption which did not recur when Plaquenil was substituted.

Schoch [6] reported on the use of Triquin in a series of 20 patients, 12 with polymorphous light eruptions and 8 with lupus erythematosus. All patients improved from 50% to complete clearing on schedules of two to four tablets daily. In seven cases the beneficial effects were equal or superior to previous treatment with chloroquine and hydrochloroquine. Side-effects were not enough to cause discontinuance of the drug.

This is a clinical report on the use of Triquin * in 71 patients with lupus erythematosus and light-sensitivity eruptions. Comparison is made with other antimalarials also used on these patients. In addition, our results in treating patients with certain other dermatoses will be briefly presented. The average dose of Triquin was two tablets daily, although in some instances it was increased to three or four tablets daily. Many of the patients were maintained on one tablet daily. Some of the patients had been on Triquin for one and a half years. In this group of patients we have had no serious side-effects or hematological complications.

* Mr. Harold Epply, Winthrop Laboratories, Inc., supplied the medication.

Lupus Erythematosus

Twenty-four patients with lupus erythematosus were treated with Triquin. Twenty were classified as having chronic discoid, one disseminated discoid, and three systemic lupus erythematosus. Sixteen of the patients (67%) had a good to excellent response, Table 1, while eight had a poor response. Three patients complained of side-effects. The first patient developed headaches and diarrhea, which necessitated stopping the medication. However, there was a good response to the Triquin. The same patient developed headaches and nausea with chloroquine but was able to tolerate and got an excellent response with Plaquenil. The second patient had a good response but developed a temporary gastritis, which disappeared when the dose was reduced from four to two tablets daily. This same patient had protracted systemic lupus erythematosus and had not responded to chloroquine or Plaquenil alone. The third patient stopped taking Triquin after a few days because "they were too bitter." The same patient was able to tolerate and had excellent results with quinacrine, chloroquine, Plaquenil, and amodiaquin.

Table 2 shows the response to Triquin as compared to the other antimalarials taken by these patients. In 22 instances the response to Triquin was superior, in 10 instances it was equal, and in 15 instances, inferior. A comparison of side-effects is also shown in Table 2. As previously mentioned, three out of the 24 patients on Triquin had side-effects. One of these patients stopped the medication after a few days because of the taste, another patient had a good response but developed a tem-

TABLE 1.—*Results with Triquin in Lupus Erythematosus and Light-Sensitivity Eruptions*

Response, %	Lupus Erythematosus		Response, %	Light-Sensitivity Eruption	
75-100 (Excellent)	12	67%	75-100	26	83%
50-75 (Good)	4		50-75	13	
0-50 (Poor)	8		0-50	8	
Total	24 Patients			47 Patients	
Side-Effects	3			1	

TABLE 2.—*Comparison with Other Antimalarials in Lupus Erythematosus*

Triquin Response	Compared To: Chloroquine (Aralen)	Hydrochloroquine (Plaquenil)	Amodiaquin (Camoquin)	Quinacrine (Atabrine)	Total
Superior	9	5	4	4	22
Equal	5	4	0	1	10
Inferior	4	5	4	2	15
Total Patients	18	14	8	7	
Side-Effects	5	2	1	1	

porary gastritis, which disappeared when the dose was reduced, and the third patient stopped Triquin because of headaches and diarrhea. Five out of the eighteen patients on chloroquine developed side-effects (headaches and nausea, purpura, toxic eruption and poor appetite, gastrointestinal upset, diplopia, and dizziness). Two out of the fourteen patients on Plaquenil developed side-effects (hoarseness, temporary partial hair fall). One patient out of the eight taking Camoquin developed a visual disturbance. One patient out of the seven taking quinacrine developed diarrhea.

We will elaborate further on the four patients with disseminated or systemic lupus erythematosus.

Report of Cases

These patients are as follows:

CASE 1.—A 45-year-old man with disseminated discoid lupus erythematosus has intermittent fever and fatigue but a negative L. E. test. We feel he is a candidate for systemic lupus erythematosus. He had a good response to all of the antimalarials, although Plaquenil was the best. His condition tends to recur when he discontinues antimalarials. He is unable to tolerate corticosteroids because of a previous history of gastric ulcers and perforation.

CASE 2.—A 27-year-old woman with systemic lupus erythematosus of six months' duration also has arthritis and fever and a positive L. E. test. She improved about 50% while taking Triquin tablets. She is no longer under our care and when last reported she was being maintained on corticosteroids.

CASE 3.—A 52-year-old woman had protracted systemic lupus erythematosus of 37 years' duration. She has had intermittent episodes of leukopenia, as low as 3,600 white blood cell count per cubic mm. She had an excellent response to Triquin and her white blood cell count returned to normal while on this medication.

CASE 4.—A 42-year-old woman with systemic lupus erythematosus of three years' duration got a good response to Triquin, although she had a temporary gastritis on four tablets daily, which disappeared when the dosage was reduced to two tablets daily.

Light-Sensitivity Eruptions

Forty-seven patients with light-sensitivity eruptions were treated with Triquin. Thirty-nine of these patients (83%), as shown in Table 1, had a good to excellent response, and eight of the patients had a poor response. Many of the patients responded rapidly within a period of one to three weeks. Treatment had to be continued for many months in some patients to prevent recurrences. An 88-year-old man felt Triquin caused a conjunctivitis; however, he continued taking Triquin, one tablet daily, for three weeks until his eruption cleared, and during this time his eye condition subsided. No other patients complained of side-effects. Fourteen of the patients had previously been on chloroquine and eleven on Plaquenil.

TABLE 3.—*Comparison with Other Antimalarials in Light-Sensitivity Eruptions*

Triquin Response	Compared To: Chloroquine (Aralen)	Hydrochloroquine (Plaquenil)	Total
Superior	5	6	11
Equal	7	2	9
Inferior	2	3	5
Total patients	14	11	
Side-effects	2	2	

TABLE 4.—*Response to Triquin in Other Dermatoses*

	Patients	Excellent, % 75-100	Good, % 50-75	Poor, % 0-50	Side-Effects
Verrucae	10	2	0	8	0
Acne	19	1	5	13	0
Seborrheic dermatitis	3	0	0	3	0
Rosacea	3	0	0	3	0
Chronic urticaria	8	1	0	7	0
Chronic eczematous eruptions	10	1	0	9	0

Table 3 compares the results with these other antimalarials. In eleven instances the response to Triquin was superior, in nine instances it was equal, and in five, inferior.

Two of the fourteen patients on chloroquine had previously had side-effects. One patient had a toxic eruption and dryness of the mouth and made a response to both Plaquenil and Triquin without side-effects. The Plaquenil alone was more effective than the Triquin. A second patient developed dizziness on four tablets of chloroquine daily. Later she had an excellent response to Triquin on two tablets daily, without side-effects. Two of the eleven patients on Plaquenil had previously developed side-effects. One patient had a gastric upset and another, dizziness. Both later responded to Triquin without side-effects.

Miscellaneous Dermatoses

Ayers and Ayers [12] reported on the use of chloroquine in other dermatoses. They felt that with lichen planus and verrucae the response was sufficient to encourage further investigation. To these authors it also appeared to exert an antipruritic or anti-inflammatory effect in a few cases of pruritic or eczematous dermatoses.

Triquin was tried in 10 patients with verrucae (6 patients had flat warts on the face, 1 had flat warts on the legs, 2 had multiple plantar warts, and 1 multiple subungual warts). In 2 of these 10 patients, Table 4, the warts disappeared within three to four weeks. There was no response in the other eight patients. There were no side-effects in this group of patients. To elaborate on the patients whose lesions cleared, one was a 34-year-old man who had been bothered by multiple flat warts of the face for four years. He had previous treatment with Plaquenil, which was not effective. The other patient was a 19-year-old student nurse who had been under treatment for one and a half years for hundreds of flat warts on her legs.

Nineteen patients with acne, three with rosacea, and three with seborrheic dermatitis were treated with Triquin. There was no response in the patients with seborrheic dermatitis or rosacea. Of the patients with acne, six out of nineteen got at least a temporary significant improvement. Three of these six patients had cystic acne. One patient felt it made her acne worse. The beneficial effect was apparent within two to three weeks. Most of the patients had been under treatment for some length of time with local, physical, or internal therapy before being placed on Triquin. There were no side-effects in this group of patients.

Eight patients with chronic urticaria were treated with Triquin. One of the eight patients seemed to get lasting benefit. This patient had chronic urticaria of two months' duration and had been previously treated with cortisone and antihistamines. Another patient got a temporary improvement of about 75% and then relapsed while still taking Triquin. There were no side-effects in this group. Ten patients with chronic eczematoid dermatoses were treated with Triquin. One patient got a beneficial response. This was in a 40-year-old man who had a chronic eczematoid dermatitis involving his hands, feet, and extremities,

of five years' duration. He had an excellent response on two to three tablets daily. His eruption tended to recur when the medication was stopped. He felt that Triquin was better than corticosteroids with which he had previously been treated.

Summary

Triquin, a combination antimalarial compound composed of Aralen, Plaquenil, and Atabrine, was evaluated in 124 dermatological patients. Response to Triquin in 24 patients with lupus erythematosus and 47 patients with light-sensitivity eruptions was felt to be comparable to the antimalarial drugs used alone. In addition, the incidence of side-effects appeared to be lower with Triquin. Response to Triquin in other dermatoses was generally poor, although further evaluation might be carried out in patients with cystic acne and verruca plana.

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Observations on the Critical Margin for the Complete Excision of Carcinoma of the Skin

GILBERT A. BEIRNE, M.D., and CLINTON G. BEIRNE, M.D., San Francisco

Carcinomata of the skin can be treated dermatologically by means of x-ray, radium, surgical excision, or curettage and desiccation. With any of these methods, it is important to remove not only all of the tumor tissue but, if recurrences are to be prevented, a certain amount of carcinoma-free tissue as well. The present study was undertaken to determine how much healthy tissue must be removed in such cases to insure an adequate margin of safety. The subjects consisted of 169 patients with basal- or squamous-cell carcinoma of the skin treated by curettage and chemosurgery in the Dermatology Clinic or in private practice during the past six years. None had evidence of metastases. In each case layers of tissue were removed from the malignant area until microscopic examination of the excised material showed no further evidence of carcinoma. Since the extent of the lesions can usually be determined with accuracy by the clinical eye and "educated" curet, an attempt was then made to correlate the extent as established microscopically with the clinical impression.

Procedure

Ordinarily, after the tumor tissue has been removed by curettage, the entire surface of the open wound is desiccated or cauterized chemically with phenol or trichloracetic or dichloracetric acid. The cauterized base is then removed, and the wound is again cauterized. Antiseptics are applied subsequently during the period of secondary healing.

The method employed in the treatment of our 169 patients, which differs slightly, is as follows: After application of a local anesthetic, the bulk of the tumor tissue, which is yielding in most instances, is removed with a sharp curet until resistant tissue, indicating collagen tissue rather than carcinomatous cytoplasm, is met on all margins. (Admittedly, this is not possible when the lesion is in direct continuity with subcutaneous fat.) An effort is made to remove all tumor possible, including extensions of undermining lesions. Hemostasis is accomplished with dichloracetic acid. Immediately thereafter, zinc chloride fixative (consisting of a 20% solution of zinc chloride made up to a thick paste with Stibnite [inert] and an emulsifier Sanguinaria) is applied to the curetted area. On the following day the layer of fixed tissue is excised in continuity from skin edge to skin edge. Its entire undersurface, prepared as horizontal frozen sections, is examined microscopically for evidence of residual carcinoma. When carcinoma is present, the fixative is again applied but to the carcinomatous areas only. These areas are excised on the following day, and again the undersurface of the removed tissue is examined microscopically. This procedure is continued daily until a cancer-free plane is reached. The layer excised each day is approximately 1 mm. in thickness, although on occasion it may be 2 mm. Since this tissue is edematous, probably no more than 2 mm. of actual tissue is removed at any one time.

Results

In 89 of the 169 cases a cancer-free plane was reached with the first excision, and in 45 cases with two excisions. Three excisions were required in 21 cases, in several of which the tumor was on the nose or ala. For cosmetic reasons, removal of tissue in these sites is made with great attention to tissue sparing. In the remaining cases four excisions were required in five instances, five excisions in four, six excisions in two, seven excisions in two, and fifteen excisions in one. In the latter case, the lesion was a squamous-cell carcinoma of the ear, which had a deep strand extending toward the canal. Even in this case it was not neces-

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From the Subdepartment of Dermatology of the Department of Medicine, University of California School of Medicine.

sary to excise the entire cavity 15 times, only the deep extension.

No recurrences have been noted in any of these patients during periods of observation ranging from two to six years.

Comment

In the majority of our 169 cases a tumor-free plane was reached after two or three excisions of the lesion, with removal of a layer of fixed tissue 1 to 2 mm. thick at a time. Five to seven excisions were required, however, in cases in which the tumor had deep extensions. Such extensions are frequently found in lesions on the nose, most of which are carcinomata of adnexal origin. In general, the lesions requiring the greatest number of treatments, as might be expected, were recurrent or sclerosing carcinomata (which some dermatologists prefer to treat by surgical excision and primary closure). Although it would appear that destruction of 1 cm. of tissue in all directions would be required to reach a tumor-free plane in such instances, actually it is rarely necessary to make multiple excisions of the whole cavity of the tumor. After the direction of the extension is determined, further excision is limited to the carcinomatous area. This is exemplified in our group by the case of squamous-cell carcinoma which required 15 excisions before a cancer-free plane was reached. The results in this group of patients indicate that, when practical, at least 0.5 cm. of tissue in all directions should be removed and that removal of 1 cm. gives almost complete certainty of cure.

Summary

A total of 169 patients with basal- or squamous-cell carcinoma of the skin were treated by curettage and chemosurgery. A layer of fixed tissue 1 to 2 mm. in thickness was excised at a time. The undersurface of the tissue was examined microscopically after each excision for evidence of residual cancer. Excisions were repeated until a tumor-free plane was reached. In the majority of the 169 cases two or three excisions were sufficient, although five to seven were required in some instances. In one case of squamous-cell carcinoma with a deep extension, 15 excisions were made. There have been no recurrences to date in these patients after two to six years of observation. These results are consistent with those obtained with other accepted dermatologic methods and indicate that effective treatment of carcinomata of the skin by any procedure requires removal of a margin of healthy tissue 0.5 to 1 cm. deep in all directions.

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Clinical Notes, New Instruments and Techniques

Tinea Capitis

Effects of Nutritional Status

EDWARD H. MANDEL, M.D., New York

A relationship between tinea capitis and nutritional status has been suggested by a recent survey among natives of the Belgian Congo. The disease was found to occur more frequently among children from communities in which the diet was low in proteins and was detected in 45 of 49 children under treatment for a protein-deficiency disease (kwashiorkor).[1-3]

A survey was made of cases of tinea capitis seen at the Children's Center, (1 E. 104th St., New York) during a one-year period, 1957-1958. The Center, a unit of the Department of Welfare of the City of New York, admits neglected children from economically deprived homes for temporary shelter. At the Center, they receive a diet which meets established standards of vitamin, caloric, and protein intake and are under medical supervision.

On admission, the children are given routine medical examinations which include inspection of their scalps. At regular intervals thereafter, the scalps are examined under the Wood's light. Clinical diagnoses of fungus infections are confirmed by culture on Sabouraud's medium.

From Aug. 30, 1957, to Aug. 30, 1958, twenty-five cases of tinea capitis, Microsporum audouini type, were seen at the Children's Center. Of these cases, two were diagnosed prior to admission to the Center and nine were detected on admission. The remainder of the children (14) became infected after having been at the Center from 2 to 10 months, during which time they were receiving nutritional and medical supervision. The two boys diagnosed as having tinea capitis prior to admission had contracted the infection while at another institution. Of the eight boys whose cases were diagnosed on admission, two were brothers.

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Summary and Conclusion

Of 25 cases of tinea capitis diagnosed at the Children's Center during a one-year period, 14 developed in children who had been at the Center for periods from 2 to 10 months. Since nutritional standards at the Center may be presumed to be superior to those to which the children had been exposed previously, some other factor, perhaps intimacy of contact, would appear to be operative in these cases.

532 Park Ave.

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Effect of Prednisolone on Geographic Tongue

HANS F. KIPPING, M.D., Buffalo

Transitory benign plaques of the tongue, a disease of unknown etiology, is refractory to therapy and tends to persist. Previous reports in the literature do not indicate a familial pattern.

This is a report of a 28-year-old woman with a 14-year history of geographic tongue. Both her mother and her 3-year-old child had this condition. The patient was treated with prednisolone for a moderately severe erythema multiforme. After three weeks of therapy, she volunteered that this was the first time in 14 years that her geographic tongue had completely cleared.

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1275 Delaware Ave. (9).

The Effect of Systemic Chloroquine Therapy on Actinic Keratoses

Report of Two Cases in Albino Negroes

JOHN M. KNOX, M.D., Houston, Texas, and CAPT. JERE D. GUIN (MC), U. S. A. F.

One of the problems in persons with "chataigne," or farmer's, type of skin is the continuous development of senile keratoses and the frequent malignant transformation of these keratoses following chronic exposure to sunlight. Recent experience with two patients suggests that chloroquine may be a partial inhibitor of this process.

The usefulness of antimalarial drugs in the treatment of lupus erythematosus has been known for several years now.[1] More recently, these drugs have been found to be effective therapeutic agents for polymorphic light-sensitivity eruptions.[2,3] In 1957, two albino Negro women reported to the Dermatology Clinic at Jefferson Davis Hospital for treatment of discoid lupus erythematosus and a chlorpromazine photosensitivity, respectively. Both had advanced actinic degeneration and numerous senile keratoses in exposed areas. The patients were followed at regular intervals for the keratotic lesions, as well as for their primary condition.

Report of Cases

CASE 1.—This 42-year-old albino Negro woman was first seen on March 1, 1957, at which time she presented several plaques of discoid lupus erythematosus on the face. In addition, she had numerous actinic keratoses on the face and forearms. The laboratory data were as follows: chest x-ray, negative; hemoglobin, 14.4 gm.; white blood cell count, 10,000, with a differential of 24% neutrophils, 73% lymphocytes, and 3% monocytes. The total protein was 8.4 gm/100 cc., and the albumin was 5.4 gm/100 cc. L. E. preparations were negative. A biopsy specimen of one of the plaques on the face was interpreted as discoid lupus erythematosus.

The patient was given a 250 mg. tablet of chloroquine daily, and her course was followed at two- to four-week intervals. Both the L. E. lesions and the actinic keratoses improved markedly during the first several months, and by Aug. 9, 1957, regression of the keratoses was estimated at 60%-70%. By February, 1958, the plaques of lupus erythematosus had completely subsided and the keratoses had undergone approximately 80% regression. There has been no essential change since February, and, to date, the patient has had no side-effects attributable to chloroquine therapy.

CASE 2.—This 43-year-old albino Negro woman had been treated for several years in the Dermatology Clinic for multiple senile keratoses. In April, 1957, she developed a chlorpromazine-induced light-sensitivity dermatitis of the forearms and face. The chlorpromazine was discontinued, and she was placed on 250 mg. of chloroquine daily. The topical lubricant was purposely not changed, so that the course of the keratoses might be followed during chloroquine therapy. The eczematous lesions cleared in two to four weeks, and the kera-

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From the Department of Dermatology, Baylor University College of Medicine (Everett R. Seale, Chairman).

toses also improved until August, 1957, when regression of these lesions seemed to become stationary. The total regression at that time was considered to be approximately 50%. The patient has continued to take 250 mg. of chloroquine daily up until the present time. The size and number of the actinic keratoses has not changed over the last several months.

Comment

These two patients have had pronounced actinic degeneration and numerous senile keratoses in light-exposed areas for many years. Incidental to the therapy of their light-sensitivity dermatoses, regression of the keratoses was observed. This regression was more noticeable during the first three to four months that the patients were on the medication. It then tapered off, becoming stationary approximately six months after treatment was started. Equally important to the regression of keratoses is the fact that there has been no progression in a usually progressive disease condition. It is doubtful that the improvement could be attributed to topical medication, since one patient used the same topical lubricant for a long period prior to the onset of antimalarial therapy. Also, such regression has not been obtained in other patients on topical therapy alone.

About 20 patients with severe actinic degeneration and numerous senile keratoses were placed on 250 mg. of chloroquine daily because of the above observations. Though not dramatic, the results in some of these patients were encouraging. Regression of keratoses was obtained in a number of persons, and the usual progression seemed to be inhibited in others. There were no noticeable changes, however, in many of these patients. Carefully controlled experimental and clinical studies were begun, because these observations may or may not have been valid. Albino mice were utilized in the experimental studies for the production of ultraviolet light-induced skin cancers. Antimalarials decreased the carcinogenic effect of hot-quartz ultraviolet light in these animals.[4] In the clinical study, 200 patients have been selected by the random-sampling technique, with 50% being given 250 mg. of chloroquine daily and 50% receiving placebos identical in appearance. This is to be a long-term evaluation, and complete results will not be available for some time.

Summary

Two albino Negro women with numerous senile keratoses and marked actinic degeneration of the skin were treated for about one year with chloroquine, 250 mg. daily.

Regression of the actinic keratoses was moderate in one patient and marked in the other. This regression was more prominent during the first several months of therapy.

Additional clinical and experimental observations tend to support the suppressive effects of chloroquine on the production of actinic keratoses.

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Dermatitis from Thermoplastic Tape

HANS F. KIPPING, M.D., Buffalo

The use of a hot-iron tape patch has become increasingly popular. The patch is applied to the torn material, a hot iron applied, and the clothing is ready to be worn (Fig. 1). Thermoplastic tapes consist of cloth impregnated with a vinyl resin, a stabilizer, and a plasticizer. The exact formulation was not divulged by the manufacturer. Previous dermatitis due to thermoplastic tape has not been reported.

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Report of Case

The patient, a 55-year-old janitor, developed a dermatitis on his back three weeks after repairing

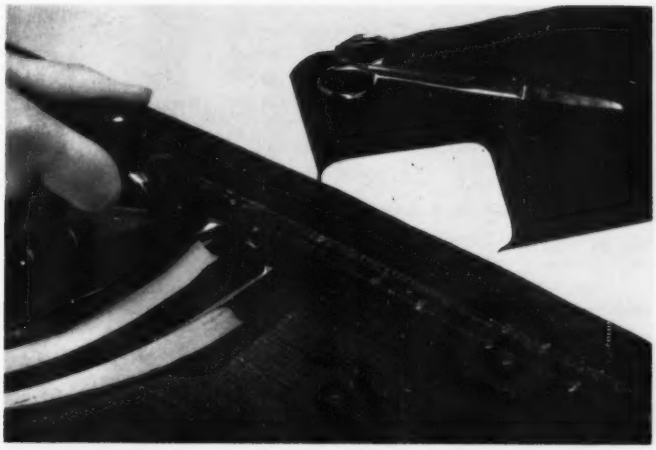

Fig. 1.—Applying thermoplastic tape.

Fig. 2.—Dermatitis located in area adjacent to patch.

Fig. 3.—Tape applied to inner surface.

his torn shirt (Fig. 2) with a thermoplastic tape. He was patch tested to the laundered tape. It was felt that laundering would eliminate the sizing or finish of the tape and rule this out as an etiologic agent. There was a 2+ reaction to the laundered tape after 48 hours.

Comment

This is a report of a case of dermatitis resulting from a thermoplastic tape. It is possible that in the manufacturing process the vinyl resins were incompletely cured.[1] There have been reported cases of dermatitis due to plasticizers and stabilizers after use of vinyl resin wrist-watch straps. These chemicals are also used in the manufacture of thermoplastic tapes.

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Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

Samuel M. Bluefarb, M.D., President
Frederick J. Szymanski, M.D., Secretary

May 21, 1958

Porphyria Cutanea Tarda. Psoriasis. Presented by Dr. Otto C. Stegmaier.

History: A 44-year-old white man was first seen on May 6, 1958, because of a chronic scaling dermatitis of the scalp. At that time it was noticed that he had a purplish pink color of the face and "V" of the neck. Further questioning revealed a history of vesicular eruption of the dorsa of the hands and arms last summer. He has noted that his urine was darker than usual. He consumes about three beers a day. He is a bartender.

Examination: Diffuse dermatitis and adherent scaling of the scalp were seen. The head, neck, and "V" of the chest reveal a pinkish hue. Over the dorsa of the hands and lower two-thirds of the arms there are scattered red depressed macular and linear areas (linear areas due to "dog scratches"). Examination of the abdomen did not reveal any enlargement of the liver.

Exposure of the upper abdomen to 30 minutes of black fluorescent (3,200 to 3,800 A.) light at 5 in. distance failed to produce any blisters or eruption at the end of 24 and 72 hours.

Laboratory findings: Urine revealed a pinkish fluorescent, which was contained in both the water-soluble and the ether-soluble portions of the urine. Urine exposed to sunlight produced an intense red darkening.

Discussion

Dr. Henry E. Michelson, Minneapolis: I just want to say a word about the prognosis in the case of cutanea tarda type of porphyria. It has been my experience, and I have seen a goodly number of such cases, that they remain fairly benign and the majority seem to get well eventually without any particular treatment. None of the treatments suggested have been successful, as far as I know, and it is interesting that some of the drugs that have been used are photosensitizing in themselves.

Dr. Allan L. Lorincz: I should like to caution against the administration of antimalarials such as chloroquine to patients with porphyria. These drugs are capable of hazardously provoking this metabolic disorder.

Dr. Theodore Cornbleet: Chlorpromazine is another agent which has been recommended in the treatment of porphyria and reported as successful. However, chlorpromazine can produce liver damage.

Dr. Arthur L. Shapiro: One would not ordinarily expect that porphyria would respond to the antimalarial drugs because of the difference in the absorption spectra of these agents and of the sensitivity spectrum in porphyria.

Dr. Otto C. Stegmaier, Davenport, Iowa: The reason I presented this patient was to reemphasize that porphyria cutanea tarda is not too uncommon, and I believe most of us should see about one case a year. That has been my average in the last six years. In the smaller areas not near a teaching center, such cases should be presented to the hospital staffs to educate the nondermatologists.

Again I should like to reemphasize Dr. Michelson's remarks that the hepatotoxic factors are the main offenders. Treatment consists primarily in keeping the patients away from alcohol and barbiturates. My seven patients in the past six years have recovered by avoiding alcohol and barbiturates without any other treatment.

I should also like to reemphasize certain things about the antimalarials. Quinacrine (Atabrine) and chloroquine should not be used in the treatment of porphyria. I have noted six acute flare-ups of porphyria caused by the antimalarials in the literature. I think this is true with any drug which concentrates too a large extent in the liver. The antimalarials concentrates 500 to 600 times the plasma level in the liver. Recently, I tried to reproduce this condition artificially. Apparently only one man, Remington, has been able to produce edema by exposing the skin to the longer wave lengths of artificial ultraviolet, but no one has been able to produce blisters by artificial means.

Submitted for publication July 17, 1958.

I exposed this patient to 30-minute exposure of black fluorescent light and to Wood's light, without the production of any blisters.

Cold Urticaria. Presented by DR. H. M. BULEY, DR. BRIAN POTTER, and DR. RICHARD REINERTSON (by invitation).

History: A white woman, aged 22, has since birth been subject to the development of red welts in her skin on exposure to a fall in air temperature. The eruption recurs almost daily but varies in intensity. The lesions are distributed chiefly over the arms, legs, and buttocks, the rest of the trunk usually being spared. If the patient clothes herself well, the covered parts are less affected. When her bedroom is particularly cold at night, she awakens with bloodshot eyes. The eruption persists for about four hours, and as it subsides the lesions tend to coalesce. There is no pruritus, but some dull, deep pain is associated. When the eruption is severe, the patient chills and becomes feverish, her temperature sometimes reaching 104 or 105 F. The eyelids, fingers, and feet swell with a severe eruption, and she may have some difficulty in breathing.

The patient's daughter, aged 6 months, has shown similar lesions since the second or third day of life, with a like distribution except that the face as well is often affected. No other members of the family have been affected so far as the patient knows. She had one transitory episode of rheumatic pain in childhood but no arthralgia before or since.

Examination: On examination the patient and her daughter present, chiefly on the arms, legs, and buttocks, an eruption of discrete but somewhat ill-defined, rose-colored edematous papules.

Laboratory findings: Hemoglobin 11.9 gm., red blood cells 4,180,000, white blood cells 8,500.

No immediate or delayed reactions were provoked by: (1) application of ice cubes to abdomen and thigh for 30 seconds; (2) immersion of hand and wrist in water at 14 C for one minute. (3) intradermal injection of 0.1 cc. 1:50,000 nicotine picrate.

The mother showed cryoglobulin negative; cold hemagglutination 1:64 (normal 1: less than 32).

The daughter was cryoglobulin negative, cold hemagglutination negative.

Biopsy of a lesion from the arm shows a primary vascular inflammation with congestion and mural and perivascular edema and eosinophil extravasation, more marked than in ordinary urticaria.

Cholinergic Urticaria. Presented by DR. DOROTHY WINDHORST (by invitation) and DR. ROGER PEARSON (by invitation).

History: A 30-year-old efficiency engineer first noted small transitory itchy papules six months ago. These usually appear all over his body in the morning after breakfast and disappear sometime before or during the following night. In the last three months he has had almost daily episodes. He finds that heat (hot showers), exercise, and excitement regularly produce attacks.

The patient has never had any previous skin trouble, and his general health is excellent.

Examination: On examination, there were numerous discrete, 3-4 mm. pale papular wheals usually surrounded by erythema ranging out 1-2 cm. and having indistinct margins. These lesions were scattered over the entire body surface, except for the palms, soles, and genitalia. General physical examination was within normal limits.

There was no dermographism. Five to ten minutes after 0.1 cc. of 1:50,000 nicotine picrate was injected intradermally typical small papular wheals were seen in the surrounding area.

Laboratory findings: Hemoglobin was 14.7 gm.; white blood cells, 15,800, with differential showing polymorphonuclear cells 75%; small lymphocytes 20%; monocytes 1%; eosinophils 1%. Urinalysis was within normal limits. Kahn test was nonreactive. Chest microfilm was negative.

A biopsy section is presented. It shows edema of the upper corium and mild inflammatory changes confined to the blood vessels. There is moderate vascular congestion, mural and perivascular edema and infiltration of eosinophils.

Discussion

DR. ROBERT W. GOLTZ, Minneapolis: We had the privilege of studying a case of cold urticaria at the University of Minnesota just last week. Dr. Milton Orkin, of our staff, was able to transmit the sensitivity by passive transfer to a normal volunteer and was also able to produce reverse passive transfer. That is, he exposed the volunteer to cold first, and then several hours later injected serum from the patient and produced an urticarial wheal at the site of cold exposure.

DR. ALLAN L. LORINCZ: The case of cholinergic urticaria presented is truly a classical example of that disease. Persons with this disorder apparently liberate no more acetylcholine in their skins in response to heat, exercise, or emotional tension than do normal persons. They, however, react abnormally by some unknown mechanism, which eventually leads to histamine release and formation of characteristic tiny wheals, to this normally liberated acetylcholine.

Any testing procedure which will activate the cholinergic innervation of sweat glands can elicit wheals in this disorder. The intradermal injection of dilute nicotine salt solutions (e. g., nicotine picrate 1:75,000) is such a procedure and normally

induces a zone of surrounding axon reflex sweating. In patients with cholinergic urticaria, tiny, so-called satellite, wheals also appear in this zone. Skin-testing for cholinergic urticaria by means of this nicotine test appears more satisfactory than the usual tests with injections of cholinergic drugs because there is no confusing direct local whealing and the nicotine salt solutions are very stable even after autoclaving. A precaution to be observed in any kind of skin testing for cholinergic urticaria is to avoid testing during a refractory period which may last for many hours after severe outbreaks of the lesions.

The question arises whether or not in cholinergic urticaria there is true allergy on the basis of an antibody reaction directed against as fundamental an endogenous metabolite as acetylcholine. I believe the answer is no, because this type of urticaria cannot be passively transferred and the reaction is readily inhibited locally by prior intradermal injection of atropine.

DR. LOUIS RUBIN, Rockford, Ill.: Regarding the case labeled "Cold Urticaria," I should like to ask if this is the diagnosis and, if so, how one can explain the absence of reaction to ice water and ice cubes.

DR. H. M. BULEY: I wish to apologize for the fact that our case was not worked up as thoroughly as it should have been. Lack of time did not allow us to do so, since we were anxious to present the case before the summer recess.

From the clinical picture of the case I was not sure at all whether or not we were dealing with "cold urticaria." We labeled the case in this manner because at the moment we had no better term for it. Certainly, the patient never showed the typical signs of urticaria. There was no wheal formation nor itching. The patient complained of "hurting" rather than itching, and the lesions were blotchy erythemas rather than urticae. The term polymorphous cold eruption, analogous to polymorphous light eruption, would, perhaps, be a better one for this disease, especially since all evidence for an allergic process is lacking.

DR. BRIAN POTTER (by invitation): The first case corresponds almost exactly with previously reported cases of congenital (familial) cold urticaria. This differs from the commoner acquired type of true urticaria, in which itching wheals are produced by actual contact with cold surfaces, such as by brushing snow off a windshield with the hand and developing hives on the palm.

In this patient the eruption tends to be produced by a cool wind or a fall in air temperature, particularly in cool humid weather. The lesions are nonpruritic, erythematous, and papular and persist longer than true wheals. Arthritis is usually associated but is not in our case.

Lupus Vulgaris. Presented by DR. SAMUEL BLUEFARB and (by invitation) DR. F. DUNLAP and DR. J. HASEGAWA.

This patient was presented before the Society at the February, 1958, meeting as a diagnostic problem. A small papule appeared on the left side of his nose approximately 16 months ago. New lesions appeared and coalesced. Yellowish and bloody drainage was noted intermittently. The lesion was relatively painless.

Past history revealed several episodes of corneal ulcers during his teens and an attack of keratoconjunctivitis on the boat home from service in Germany (six to eight weeks prior to appearance of the nasal lesion). A cough productive of yellow and dark sputum had been present for eight months.

Family history: One brother had been hospitalized in 1955 for pulmonary tuberculosis. His father died 17 years ago of diabetes. Drug history revealed a rather constant intake of proprietary drugs, including 666. When he first applied for admission at the Veterans Administration Hospital, on March 14, 1958, he stated that all such drugs and alcohol had not been taken for the preceding five months.

Laboratory findings: Hemoglobin 13.4 gm.; hematocrit 44%; white blood cell count 6,400; sedimentation rate 33 mm.; VDRL negative; ASO titer 320 Todd units; eosinophil count 44 per milliliter; total proteins 8.2, with albumin of 4.9; urinalysis normal. Stools for ova and parasites negative three times. Fasting blood sugar 92.5 mg.; serum bromide 3/20-25 mg. %; 3/27-16 mg. %; 5/14-22 mg. %.

Routine bacterial cultures of the sputum and exudate from the lesion revealed normal flora. Special cultures for fungus and Leishmania were negative. Smears were negative for acid-fast bacilli. Guinea pig inoculation for acid-fast bacillus (nasal tissue) was negative. Cultures of the sputum and the nasal lesion exudate revealed colonies of organisms resembling Microbacterium tuberculosis. Several chest x-rays were negative for pulmonary infiltration.

Biopsy report: There is a small portion of skin with moderately thickened stratified squamous epithelium. The rete pegs are elongated, and there is considerable lymphocytic infiltration in the subepithelial zone. Few granulomatous-like nodules with some large epithelioid cells are observed. The PAS and AFB stains are negative for specific organisms.

The patient has been on isoniazid and streptomycin for eight weeks, with a rather marked response. Tuberculin skin test (intermediate strength) was markedly positive (necrotic reaction). Fungal skin tests were negative.

Discussion

DR. HENRY E. MICHELSON, Minneapolis: I want to discuss this patient because I do not like to see some of the younger men go away with the impression that lupus vulgaris looks like the presented case. I cannot offer a substitute diagnosis, but one thing is certain—that when tuberculosis is present clinically it is also microscopically, and there was no tuberculoid structure in these sections.

I noticed, too, the patient received INH and streptomycin. I think most of the Continental dermatologists who have charge of treating lupus vulgaris reserve streptomycin for resistant cases, and I do not think it is a good practice to give it firsthand. The INH should be given a chance. This is aside from the present case. Also, one must realize that INH therapy is not specific.

DR. SAMUEL BLUEFARB: Culture of the sputum was positive for acid-fast organisms.

I believe you will recall that this patient was presented a couple of months ago as a possible example of "bromoderma." He had approximately 25 mg. of bromine in the peripheral blood.

DR. F. DUNLAP (by invitation): Really, I have no stand to take as far as what Dr. Michelson has said. This man was given, previous to our care, various courses of antibiotics, including tetracycline, and received no help from them.

For the first two or three weeks under our care we noted that the lesion continued to spread, although very slowly.

Cultures for acid-fast organisms came back positive, one from the sputum and one from the drainage from the nasal lesion. Dr. Silverman, our bacteriologist, said they looked like M. tuberculosis. He has pointed out to us that a large amount of work is being done on so-called atypical acid-fast bacilli and brought to our attention a reference by a man named Griffith, who in 1924 showed that the acid-fast bacilli which can sometimes be grown from lupus vulgaris is not particularly pathogenic for the guinea pig. Runyon in his work classified some 88 atypical acid-fast bacteria into three groups according to cultural and morphological characteristics. All 88 strains were grown from people with chronic lung disease resembling tuberculosis. None of these are pathogenic for the guinea pig, but all strains in Group 2 are pathogenic for mice. What all this means in this particular patient, I do not know, except that we may postulate that this is an infection with a so-called atypical acid-fast bacterium.

Telangiectasis Macularis Eruptiva Perstans. Presented by DR. ADOLPH ROSTENBERG JR. and (by invitation) DR. J. FOX.

History: A 44-year-old white man was admitted to the Hines Veterans Administration Hospital with a history of diffuse involvement of the skin for 10 years. The lesions are dark red macules located particularly over the face, arms, and trunk. They began as small macules on the face and gradually spread to the trunk, arms, and neck area. The patient had a bilateral sympathectomy performed for Raynaud's phenomenon of the hands. The patient states his feet and hands are still uncomfortable during the winter months. He states there has been no sweating of the upper trunk, neck, or head since this operation. The only other significant past history is that the patient had painless urinary bleeding in October, 1957, and was told at that time that he did not have kidney stones. A high uric acid content was found at that time. He has had no trouble since. In 1957 the patient consulted a dermatologist for his skin condition and was put on chloroquine (Aralen), which he has been on to the present time. He feels that some of the lesions have disappeared, particularly those on his forehead and forearms.

Examination: The patient presents dark red macules and telangiectatic lesions mainly over the arms and upper trunk which blanch on pressure. The skin of the fingers is somewhat bound down. The nail beds are somewhat bluish in coloration.

Laboratory findings: White blood cells 8,700, with 64 polymorphonuclear cells, 36 lymphocytes; 14.5 gm. hemoglobin; hematocrit 49%. Sedimentation rate 2 mm. per hour. The urinalysis is entirely negative.

Nonprotein nitrogen 32.4; alkaline phosphatase 1.6; total protein 6.8; albumin 4.5 and globulin 2.3.

Urticaria Pigmentosa. Presented by DR. SAMUEL BLUEFARB, DR. SILAS WALLK, and (by invitation) DR. MARTIN L. GECHT.

Discussion

DR. M. J. BRUNNER: I should like to suggest an alternative diagnosis for the case at Illinois: that of scleroderma with telangiectatic changes. The patient has scleroderma lesions on the fingers, as well as a history of Raynaud's phenomenon in the hands. There is some sclerodermatous tightening of the skin of the face, which is most prominent in the areas of telangiectasia macularis eruptiva perstans, so-called.

DR. A. H. SLEPYAN: I think Dr. Brunner has a good point in thinking of scleroderma. However, the pattern of telangiectasis macularis eruptiva perstans is still present. I feel this pattern occurs as a result of many etiologic factors. Oppenheim

and Yacullo, in about 1941, reported in the *British Journal of Dermatology* a case report of a woman 65 years of age who showed the pattern of telangiectasis macularis eruptiva perstans for about 15 years. This eruption apparently appeared following the taking of Pyribenzamine. I have seen a 15-year-old high-school student who erupted in a similar fashion following a histaminic that was purchased over the counter for the treatment of a cold. His eruption persisted for two and one-half years. This patient has scleroderma, but the overlying picture is suggestive of telangiectasis macularis eruptiva perstans.

DR. SAMUEL J. ZAKON: What was the surgery done for?

DR. SAMUEL BLUEFARB: For Raynaud's disease.

DR. ADOLPH ROSTENBERG JR.: I should like to comment from two points of view on the case of telangiectasia macularis eruptiva perstans from Illinois. The first is, what does the patient have? The second is, what does this label mean? We saw this patient for the first time the other day, and we have had no chance to work him up. We were not sure how to label the case, but thought that telangiectasia eruptiva perstans was the best label. The suggestion made by Dr. Brunner of scleroderma is a good one.

Now, what does this label mean? It was first used by Parkes-Weber, but Colcott Fox much earlier had included this condition under the essential telangiectases. The problem is, do such telangiectases necessarily denote a specific underlying condition, such as a mast-cell disease, or can they be the morphologic expression of a variety of stimuli? I think the latter.

Lichen Planus and Psoriasis. Presented by DR. SAMUEL BLUEFARB and (by invitation) DR. F. DUNLAP and DR. J. HASEGAWA.

Discussion

DR. C. W. FINNERUD: I think it is possible in this instance to make just one diagnosis, the one that is so evident. The patient does have definite lichen planus of the skin, in the mouth and on the lips, and admittedly he has psoriasiform lesions of the elbows, the sections of which show a good picture of psoriasis. But one often sees a good histologic picture of psoriasis in lichenified plaques, so we cannot necessarily say that these changes are psoriasis. The nail changes can be due to contactants, or they can be conceived to be one of the nail changes of lichen planus. I think this patient has only lichen planus.

DR. ANTHONY C. CIPOLLARO, New York (by invitation): Sometimes we are justified in making two diagnoses in a patient who presents such different lesions as this one does. The lesions on the lips and elbows and the nail changes suggest the diagnosis of psoriasis. The lesions on the lips and dorsa of the hands suggest the diagnosis of lichen planus. Histologically there is evidence of psoriasis and of lichen planus. I agree that this patient has both lichen planus and psoriasis. It is a combination which I have never seen until this afternoon.

DR. ADOLPH ROSTENBERG JR.: As someone said, we dermatologists cannot grow hairs, but we can split them. I think some of this discussion may verge on hair splitting.

The late Dr. Oliver and I showed a case of this combination a couple of years ago. There have been quite a few presented in New York. My father presented one there many years ago. Louis Brocq suggested that psoriasis and lichen planus are cutaneous reactions and by virtue of this can undergo metamorphoses, one into another. The combination of lichen planus and psoriasis happens, not commonly, but not really rarely. Usually the psoriasis antedates the lichen planus, which often develops acutely and causes the psoriasiform lesions to retreat before it. In the case we had at Hines this was demonstrated beautifully. We first saw him when the psoriasis started to recede before the lichen planus, later the lichen planus involuted and the psoriatic lesions returned.

Atypical Dermatitis Herpetiformis with Arthritis and Pyoderma Gangrenosum, Successfully Treated with Sulfamethoxypyridazine. Presented by DR. BRIAN POTTER (by invitation) and DR. FREDERICK D. MALKINSON.

(This patient was previously presented before this Society, Nov. 20, 1957, as a case for diagnosis).

A 37-year-old white woman was well until January, 1957, when she became pregnant and began taking quinine. Later in the same month a pruritic vesicular eruption appeared on the right ankle and spread to the other extremities and the trunk and persisted.

The patient aborted in March, 1957, and in the same month began to suffer from migratory joint pains.

In June, 1957, firm nodules appeared in the skin of the legs, breaking down to form ulcers. After intradermal injections of Staphylococcus toxoid, similar ulcers developed in the injection sites of her left arm and forearm.

There was a 15 lb. loss of weight in eight months. A diagnosis of rheumatoid arthritis was made, and the patient was treated with prednisone, 1-4 tablets daily, with some relief from pain but no improvement in the eruption and ulcerations.

When seen in November, 1957, she presented the vesicular eruption and several cutaneous ulcers. On each leg there were four ulcers and on the

left forearm one, each 2-4 cm. in diameter, with similar residual lesions on the left arm, right buttock, and one elbow. Each ulcer had granulating base with central epithelial islands and a spongy epithelial periphery, pale blue in color and separated from the surrounding normal skin by a narrow zone of erythema.

There was a serosanguineous exudate, with pus expressible from tiny sinuses. Cultures taken for bacteria showed no pathogens and for fungi showed no growth.

Positive findings at this time were as follows:

Examination: Palpable thyroid, liver, and right kidney. Finger joints swollen and stiff; right ankle swollen and tender.

Laboratory data: Reactive Kahn and VDRL, doubtful Eagle. Elevated serum total globulins (3.4 gm/100 ml.) due to raised α_2- and β-globulins; γ-globulins within normal limits. BMR+15. Skin tests to tuberculin, histoplasmin, blastomycin, and coccidioidin, all negative. Extensive further tests and examinations listed in the previous protocol were negative.

Prednisone therapy was continued, and at this stage the patient was presented to this Society. In the discussion acne conglobata and factitial dermatitis were the diagnoses suggested.

After the date of her presentation, the ulcers began to show central healing but peripheral activity continued. The pruritic vesicular eruption persisted, localized chiefly to the sacral area, buttocks, lower abdomen, and outer thighs, with occasional lesions on the wrists, hands, legs, and elsewhere. New lesions were tense vesicles, sometimes grouped, and subsiding to leave excoriated, occasionally crusted, pigmented scars. The clinical impression at this time was atypical dermatitis herpetiformis.

Treatment with sulfapyridine, 0.5 gm. t. i. d., for two weeks produced no subjective or objective improvement. Sulfamethoxypyridazine (Kynex, Midicel), 0.5 gm. b. i. d., however, was soon effective. No vesicles appeared while the patient took the drug, but lesions recurred on the scalp and neck three days after interruption of treatment. On reintroduction of the drug, the blistering was again controlled. Pruritus, however, was not completely relieved.

Activity of the ulcers continued and still demanded debridement of crusts after four weeks of therapy, but by the 11th week all ulcers were healed except for some localized activity at the periphery of two of them. In the meantime prednisone was discontinued after seven months of treatment, and there was no exacerbation of her arthritis. Transient arthralgia is controlled by acetylsalicylic acid, and there is no evidence of any joint deformity. The eruption is controlled by Midicel, 0.5 gm. daily.

The patient feels well and has regained 11 lb. in weight. Peripheral blood differential count gives 11% eosinophils, with white blood cell count of 9,000.

In retrospect, this case corresponds to the syndrome of atypical dermatitis herpetiformis, arthritis, and pyoderma gangrenosum described by Perry and Brunsting (A. M. A. Arch. Dermat. 75:380-386 [March] 1957), and by Ayres and Ayres (A. M. A. Arch. Dermat. 77:269-280 [March] 1958).

Color photographs of the lesions and sections from biopsies done in November, 1957, are presented.

Discussion

Dr. Anthony C. Cipollaro, New York (by invitation): This syndrome is rare, and I appreciate the opportunity of seeing this case. Dr. Maurice Costello, in New York, saw two of my cases with symptoms similar to those presented here, and he included these cases among those reported by Brocq under the name of dermatite polymorphe doloreuse. My cases responded to promacetin. I believe that these cases presented by Ayres and Ayres (Pyoderma Gangrenosum with an Unusual Syndrome of Ulcers and Arthritis, A. M. A. Arch. Dermat. 77:269 [March] 1958) belong to the same group. All these cases are probably variants of dermatitis herpetiformis, whose etiology is still obscure.

Dr. A. H. Slepyan: I find it hard to classify this patient as having dermatitis herpetiformis. All that we see now is the remains, namely, pigmentation. It appears that each and every lesion had been quite discrete, with no real tendency toward grouping. This pattern as seen today should have been caused by a pyogenic process.

Dr. Brian Potter (by invitation): It was the distribution of the vesicles in some of the areas of predilection of dermatitis herpetiformis, namely, over the sacrum and outer thighs, that suggested this diagnosis. Histologically, the vesicles containing eosinophils also made me wonder about an atypical dermatitis herpetiformis. The patient's good response to treatment was regarded as confirmation of the diagnosis.

When the paper on pyoderma gangrenosum with an unusual syndrome of ulcers, vesicles, and arthritis by Ayres and Ayres was published, Dr. Malkinson realized that their cases were similar to our patient, and looking back we found that some of the patients with pyoderma gangrenosum described by Perry and Brunsting also corresponded with this case.

Radiodermatitis with Epitheliomas. Presented by Dr. David Omens and (by invitation) Dr. Harold Omens and Dr. Hassan Yazdi.

Discussion

DR. ANTHONY C. CIPOLLARO, New York (by invitation): This patient has radiodermatitis and multiple epitheliomas.

It was formerly thought that only squamous-cell epitheliomas develop in radiodermatitis. It seems that basal-cell epitheliomas develop in radiodermatitis more frequently than squamous-cell epitheliomas. Epitheliomas or persistent radiation ulcers are best treated either by electrosurgery or by scalpel surgery.

The question was raised as to whether an erythema always precedes radiodermatitis. Not necessarily. That depends on the quality of radiation, or the thickness of the filter used. When radiations generated with 200 kv. are used, the erythema occurs much later than when radiations are produced with 100 kv. In fact, with the harder rays, the pigmentation may mask the erythema. Since dermatologists employ low voltage unfiltered x-rays, acute radiation reactions characterized by erythema and vesiculation are usually elicited early, usually within one week after exposure. When a borderline dose of soft radiation is administered, it may be difficult to elicit an erythema from a pending erythema.

The second question raised relates to the amount of radiation reaching the gonads in the course of routine dermatologic radiotherapy. We have been taking measurements at the New York Polyclinic Hospital. We found that when epilating the scalp for tinea capitis, that only 20 mr reach the region of the gonads. This is a very small amount when you consider that 1,500 r was applied to the entire scalp for this procedure. We were able to reduce this amount of 20 mr to practically zero by covering the region of the gonads with 4 mm. of lead, tilting the tube away from the gonads and using cones and x-ray leak-proof apparatus. By slight variations in technique, greater protection is afforded patients who require x-ray therapy for the treatment of stubborn dermatoses.

In treating acne with x-rays in the usual fashion, we found that with each dose of 75 r given to the face, an average of 2 mr was measured in the vicinity of the gonads. For a total of 1,200 r given to each side of the face over a period of about five months, about 64 mr reached the gonads. This, too, is a small dose which was reduced to the vanishing point by using 4 mm. of lead shielding.

When treating a plantar wart with 1,000 r, approximately 15 mr is measured in the region of the gonads. This, too, was reduced considerably by employing the precautions previously enumerated. Thus it is seen that when x-rays are employed for the treatment of a skin disease for a prolonged period of time, the amount of radiation reaching the gonads is infinitesimal.

The degrees of pigmentation following x-radiation is in direct proportion to the softness of the irradiation employed. Following the use of such soft radiations as grenz rays or thorium X, we all know that the pigmentation is intense. I know of no good treatment to hasten the disappearance of the pigmentation. In due time, it disappears pretty well. However, pigmentation following ultraviolet light disappears more promptly than that following ionizing radiations.

DR. H. M. BULEY, Champaign, Ill.: I asked the patient about past exposures to sunlight, and he told me that at the time he suffered from acne he used to take many sunbaths which always seemed to help him and was sunburned repeatedly. This brings up the question of whether there was an additive effect on his skin by the roentgen rays and the ultraviolet rays, leading to an actinic atrophy, which would not have been produced by either agent alone. Certainly repeated excessive exposures to the sun are capable of producing actinic atrophy, not only in abnormal conditions, such as in xeroderma pigmentosum, but also in normal skin.

Recently I saw a patient who had never received x-ray therapy but who, years ago, had worked on the pineapple plantations of Hawaii without protective clothing on his upper trunk. His skin now shows all the signs of an actinic atrophy with telangiectases, pigment changes, keratoses, and superficial epitheliomas.

I should like to ask Dr. Cipollaro for his opinion concerning the combined effect of x-rays and ultraviolet light.

DR. CIPOLLARO: I would agree that intense doses of ultraviolet light either natural or artificial, adds to the damage done by overexposure to x-rays. However, it is to be emphasized that radiodermatitis is essentially caused by the ionizing radiations employed rather than by the exposure to sunshine. As Dr. Michelson has said, when ultraviolet rays cause changes in the skin simulating radiodermatitis, age plays an important role. Prolonged exposure to ultraviolet light added to overexposure to ionizing radiations would produce a more intense radiodermatitis.

In this case, I believe that overexposure to x-rays is primarily responsible for the radiodermatitis we see today.

DR. ROBERT M. GOODWIN, Springfield, Ill. (by invitation): I have a question for Dr. Cipollaro. In making your measurements on the young woman described, who received a projected total of 1,200 r and which you calculated out as a projected 60 mr accumulative to the gonads, were the gonads shielded in any fashion? And where was the dosimeter placed, over the perineum?

DR. CIPOLLARO: When making our measurements, the ionization chamber was covered with

1 mm. of lead. This is the thickness of lead ordinarily employed for shielding. I think it is well to cover routinely the region of the gonads with a lead shield. Some dermatologists wrap a lead rubber sheet around the patient. I do not believe that this extreme measure is essential. We shielded the patients and took the measurements without the patients being aware of what was going on. The less we talk about radiation hazards to our patients, the better. In this way, apprehension is lessened. A lead shield over the pelvic region goes as unnoticed as lead eye shields.

DR. DAVID OMENS: I am grateful for the discussion.

Congenital Ectodermal Defect. Presented by DR. BRIAN POTTER and DR. RICHARD REINERTSON (by invitation).

Polymorphic Light Eruption—Eczematous Variety. Presented by DR. BRUCE BAIRSTOW.

Case of Ulcerating Granuloma for Diagnosis. Presented by DR. IRENE NEUHAUSER and (by invitation) DR. GEORGE FLEMING.

Kaposi's Sarcoma. Presented by DR. ARTHUR L. SHAPIRO.

Mycosis Fungoides. Presented by DR. S. BARSKY, DR. P. GRIFFITH, and (by invitation) DR. J. FOX.

Basal-Cell Nevi. Presented by DR. MARCUS R. CARO and DR. H. H. RODIN.

Familial Benign Chronic Pemphigus in Mother and Her Identical Twins Aged Forty-Three. Presented by DR. C. A. VANDER LAAN.

Pseudoxanthoma Elasticum with Marked Calcinosis. Presented by DR. SAMUEL BLUEFARB, DR. SILAS WALLK, and (by invitation) DR. MARTIN L. GECHT.

Keratoderma Plantaris? Verrucae? Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY and (by invitation) DR. J. LATONI.

Keratoderma? Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and (by invitation) DR. J. LATONI.

Nutritional Deficiency—Pellagra. Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and (by invitation) DR. MARTIN GECHT.

Congenital Ichthyosiform Erythroderma. Presented by DR. DAVID OMENS, and (by invitation) DR. HAROLD OMENS and DR. J. LATONI.

Leukonychia with Alopecia Areata. Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and (by invitation) DR. HASSAN YAZDI.

Metastatic Carcinoma—Lung? Presented by DR. SAMUEL BLUEFARB, DR. SILAS WALLK, and (by invitation) DR. MARTIN L. GECHT.

Drug Eruption—Iododerma? Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and (by invitation) DR. MARTIN L. GECHT.

Chronic Lymphocytic Leukemia with Ecchymoses. Presented by DR. SAMUEL BLUEFARB, DR. SILAS WALLK, and (by invitation) DR. HASSAN YAZDI.

CHICAGO DERMATOLOGICAL SOCIETY

Oct. 15, 1958

The Members of the Attending, Associate, and Resident Staff of the Cook County Hospital, as well as the Staff of the Cook County Graduate School of Medicine, wish to dedicate the Cook County portion of the Chicago Dermatological Society Meeting to two esteemed members of our staff who have chosen to retire from active participation in our department.

Dr. David V. Omens has been a member of the Attending Staff for the past 30 years, and Dr. Herbert Rattner has been an Attending Dermatologist for the past 18 years.

In recognition of the great contributions they have made to Cook County Hospital, we dedicate these transactions.

Samuel M. Bluefarb, M.D., Chairman
Department of Dermatology
Cook County Hospital
Karl A. Meyer, M.D.
President
Cook County Graduate School of Medicine

Telangiectasia, Calcinosis with Sclerotic Changes. Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and (by invitation) DR. I. GIGLI.

A 57-year-old white man stated that he has been troubled with "cold" hands for the past 20 years. He has previously been treated for Burger's disease and Raynaud's disease. A diagnosis of scleroderma was made in 1956. He has been a patient at another institution for the past 20 months.

His right leg was amputated in 1955 because of arteriosclerosis, and the following year the left leg was amputated. Six months after this surgery, violaceous lesions appeared on his forehead. He was treated with various medications.

He now complains of pain in both hands along the distribution of the ulnar nerve. One year ago the tips of his fingers became ulcerated and drained pus and small particles of calcium extruded from the ulcers. The skin of his hands then became thicker, there was some muscular atrophy, and he lost some weight. He is known to have an allergy to penicillin.

Submitted for publication March 23, 1959.

On examination, the pertinent findings included bilateral atrophy of the interosseous muscles of the hands, several hemorrhagic areas on the tongue and buccal mucosa, and the cutaneous lesions. There are several small red macules on the forehead, nose, tongue, and both palms. The elasticity of the skin is very poor, and the skin over the fingers is thickened. There are several areas of hypopigmentation, with some hypotrophia, on the central dorsal area of the glans penis. There were calcifications in the soft tissues.

Clinical impression was that of scleroderma.

Scleroderma. Presented by DR. SAMUEL M. BLUEFARB, DR. SILAS WALLK, and (by invitation) DR. I. GIGLI.

A 65-year-old Puerto Rican woman had noted generalized tenderness of her joints, most marked in the wrists and fingers, for one year prior to entering the hospital. She had difficulty in closing and extending her fingers because the skin was "too tight." A sensation of "cold" persisted in the hands and feet, even during warm weather. Her appetite was poor; she has lost weight and has had episodes of diarrhea and weakness.

Examination revealed that she was unable to open her mouth widely ("fish" mouth), and there were a few hemorrhagic "points" on the tongue and buccal mucosa. There were bilateral basal rales in the lungs with occasional inspiratory "wheezes," decreased breath sounds, and dullness in the right middle lobe. There were deposits of calcium on the abdominal wall, around the umbilicus, and a soft, smooth, nontender "mass," the size of a "grapefruit" in the right hypochondrium. There was limitation of motion of the extremities, as well as "claw" hand. The skin was atrophic with a loss of elasticity, and there were depigmented areas on the hands and forearms. There were monomorphous, symmetrical lesions present on the face and extremities. The skin of the face was immobile because of its "hard" consistency.

Significant laboratory findings: Serum electrophoresis: moderate increase in γ-globulin. Feces: endameba histolytica trophozoites.

Roentgenogram: Gastrointestinal tract (barium by mouth) showed scleroderma of esophagus and small intestine. Barium enema showed scleroderma.

Histological examination of the skin: Scleroderma.

Treatment has consisted of the administration of trisodium ethylenediaminetetraacetic acid.

Linear Scleroderma (Possibly Developing into Systemic Scleroderma). Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS and DR. JOSE LATONI.

An 11-year-old Negro girl first noted that the lesions appeared on her left thigh as a patch, which has gradually increased in size. These lesions were followed by similar ones on the left upper extremity and chest. Coldness and numbness of the hands were noticed a year ago. There is no dysphagia or involvement of the genitalia.

Physical examination reveals several atrophic, infiltrated, irregular, inelastic, unilateral patches, disposed in a linear fashion and involving the left side of the body.

Laboratory findings: Blood chemistry showed increased γ-globulin and thymol turbidity.

X-rays: 1. Two views of the dorsolumbar spine were normal. 2. One view of both hands: There is slight irregularity seen at the tips of the distal phalanx of the fingers. Impression: There is evidence of very early changes in the bones in the distal phalanx of the hands, suggestive of scleroderma.

Scleroderma: Progression of the Disease Over a Twenty-Eight-Year Period. Presented by DR. MILTON ROBIN and (by invitation) DR. BETSY B. BRENNAN.

This 43-year-old white, single woman has been under observation at the Research and Educational Hospitals since she was 19 years old. She presented herself at that time with the following complaints:

1. Pain and cyanosis of her fingers when exposed to cold—four years' duration.
2. Stiffness of the fingers—three years' duration.
3. Low back pain in damp cold weather—one year's duration.

Her disease has been slowly progressive since the age of 15, in spite of therapy, which has included the following procedures:

1. Partial parathyroidectomy—1935.
2. Right cervical sympathectomy—1936.
3. Left cervical sympathectomy—1939.
4. Left lumbar sympathectomy and skin graft to ulcer of the left ankle—1957.
5. Appendectomy—1936.
6. Correction of retroverted uterus—1938.

Nonsurgical treatment has included radiation to the extremities, viosterol, corticotropin, prednisolone, low-calcium diet, multiple vitamins, sodium phytate, PABA, acetylcholine, thyroid extract, prostigmine, local steroids, and antibiotics for ulcerations of extremities. A recent attempt to give edathamil calcium-disodium intravenously was unsuccessful. Because of intense pain along the course of the vein during treatment, therapy was discontinued.

At present she is troubled by stiffness of the joints of the hands, wrists, and ankles; joint pains; difficulty in swallowing; recurrent facial swelling; marked intolerance to cold, with pain and cyanosis of fingers and toes; recurrent ulceration of the lower legs; muscle weakness, and development of tender swellings around elbows which open and drain whitish material.

She is a thin, well-developed woman with a "mask-like" face and thin prominent nose. The skin of the hands is thick, bound down, shiny, and pale, with loss of normal creases. Many terminal phalanges have been lost by spontaneous amputation. The skin of the forearms and lower legs is also thick and bound down. There is an ulceration of the left lower leg. The foot is moderately contracted with slight inversion and plantar flexion. The remaining physical findings are not contributory.

This patient is presented as an example of scleroderma with symptoms at an early age and slow progression of the disease in spite of varied treatment.

Discussion

DR. HAMILTON MONTGOMERY, Rochester, Minn.: The dermatohistopathology of various types of scleroderma cannot be accurately distinguished one from another, though there are certain minor variations as I pointed out in the paper with O'Leary and Ragsdale (A. M. A. ARCH. DERMAT. 75:78-87 Jan. 1957). Localized forms, especially morphea, show more of an inflammatory reaction and less vessel changes. Acrosclerosis reveals relatively little inflammation and relatively little increase in collagen. Diffuse generalized scleroderma, which is the most serious type in regard to prognosis, histologically shows the greatest change in the blood vessels in the skin, and also in the interceptal vessels in the muscle. In children, as Christensen has pointed out, there may be linear scleroderma with hemiatrophy.

DR. M. R. CARO: I was particularly intrigued by the cheesy articular nodes that were present in the first case at the Cook County Hospital. I have never seen them so markedly calcified or so large in a patient with scleroderma.

DR. THEODORE CORNBLEET: We selected the title of presentation for one of our patients to emphasize the manifold way scleroderma may display itself, especially early in its course. A localized calcinosis may portend a scleroderma, localized or extensive. Progression and spread may develop so slowly as to go unnoticed and be deceptive. It may invade the skin from the viscera. There are sclerous processes of the acrae, which probably are unrelated to scleroderma, but where they end and the latter begins is hard to say and is a matter of opinion. There are no solid criteria of corroborating a clinical judgment. The histological changes are probably not specific and often are inconclusive.

The dimness of prognosis in general parallels the extent of skin involvement, unless visceral involvement belies it. Kidney changes make the outlook graver, and cardiac changes, either primary or secondarily as a cor pulmonale from pulmonary changes, are unfavorable for the patient's future. I have watched the patient presented by Dr. Robin for 20 years. She had the classical form of the so-called acrosclerosis. Its prognosis for eventual arrest is usually good.

Periarteritis Nodosa(?). Presented by DR. SAMUEL M. BLUEFARB, DR. SILAS WALLK, and (by invitation) DR. RICHARD I. BERNSTEIN.

A 28-year-old Negro woman was first examined because of a dry gangrene which had been present for the previous three weeks. There was involvement of the fingers of the right hand, the index finger of the left hand, and the heel of the right foot, and there was a small oval-shaped area on the right side of the chest. The day preceding onset of the gangrene she had a temperature of 105.6 F, bilateral costovertebral angle tenderness, and pain on urination. She was given sulfisoxazole (Gantrisin) and tetracycline, and the temperature became normal in 24 hours. Ecchymoses had been noted in the involved areas preceding the onset of the gangrene.

About 10 months previously, she gave birth to an infant six weeks prematurely (her two other children had been of nine months' gestation). During the last pregnancy she lost 40 lb. in weight, and during the month after delivery she noted weakness and paresthesias, most marked on the left side of the body. Subsequently, she had three convulsions. Angiograms were then done, but the findings were not specific. However, there was an absence of the left carotid pulse. She is known to have an allergy to penicillin but has received neither penicillin nor any ergot preparations recently.

On examination her blood pressure was 90/60 on one occasion and 122/78 on another. The liver was palpable 4 fingerbreadths below the right costal margin, and she complained of pain and tenderness of the right upper quadrant. She also complained of pain in the areas of gangrene. There was a Grade 2 systolic murmur at the cardiac apex. A few "moist crackling" rales were noted at the base of the lungs. Both radial pulses were palpable. Although this patient has a dark skin, it has an irregular, dark, hazy appearance which is suggestive of incipient gangrene.

Significant laboratory findings: Urinalysis: Specific gravity 1.010-1.014 (three examinations); albumin 2+; on microscopic examination, hyaline and granular casts and red and white blood cells.

Discussion

DR. HAMILTON MONTGOMERY, Rochester, Minn.: The term "periarteritis nodosa" usually implies a very grave disease with fatal prognosis. We have had five cases of periarteritis nodosa, four of which were limited to the skin. One patient many of you saw a good many years ago at Hines Hospital. He was a veteran who had cutaneous

periarteritis nodosa and is alive and well 17 years later. Just as we see sarcoid limited to the skin and lupus erythematosus in the discoid form limited to the skin, one can have cutaneous periarteritis nodosa histologically indistinguishable from the systemic forms and which may run a benign course. It may possibly be on an allergic basis, though I do not like the term "allergic angiitis," which has been employed by Zeek and also by Ruiter. Nevertheless, this term or some modification thereof is better than to use the term periarteritis nodosa and, thus, scare both the patient and the physician.

DR. S. J. ZAKON: In the 1940's, when sulfonamide preparations were used much more extensively than now, the incidence of periarteritis nodosa was greater. With the decrease in the use of sulfonamide, the incidence of periarteritis nodosa decreased. There seemed to be a definite relationship between the widespread use of sulfonomide preparations and the incidence of periarteritis nodosa. This patient was taking sulfisoxazole.

Lichen Sclerosus et Atrophicus. Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS and DR. CHESTER L. KROLL.

This 67-year-old white woman came to the dermatology clinic of Cook County Hospital because of an abrasion of the right breast following trauma. Upon examination, it was noted that the skin of the areolae of both breasts was atrophic, wrinkled, and white and had a "tissue-paper-like" appearance, with scattered pinkish areas. She does not recall the duration of this condition.

Lichen Sclerosus et Atrophicus. Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and (by invitation) DR. JOSE LATONI.

A 36-year-old white man first noted cutaneous lesions four years ago. These lesions consisted of a small white, papular "patch" on the back, which has undergone evolution, increased to present size, and become atrophic. There is no involvement of the genitalia or perianeal areas, and no subjective symptoms have been present at any time.

There is a 3 cm. erythematous, scaly, pruriginous "patch" which has been present on the left arm for one year.

The histologic section of the lesion on the back, which is presented, shows changes consistent with this diagnosis.

Case for Diagnosis. Presented by DR. MALCOLM C. SPENCER, Danville, Ill.

A white man, aged 23 was seen for the first time on Oct. 8, 1958. He had a history of about three years' duration, or since marriage. A biopsy was performed two years ago, by a urologist and was reported as leukoplakia of urethral meatus, Grade I. The patient has noted occasional dysuria and deflecting of urinary stream since biopsy was done. No treatment has been used. He does not feel that there has been any significant change during the last two years.

Examination reveals narrow, whitish, slightly infiltrated band surrounding urethral orifice. There was no regional adenopathy. The rest of the cutaneous surface is clear.

Biopsy specimen of 1956 is presented.

Discussion

DR. M. J. REUTER, Milwaukee: The condition is usually considered a banal disease. However, in the past few years in my practice two women with involvement of the anogenital area have developed highly malignant carcinoma of the labia. That may be one of the coincidences in medicine.

As to the patient with the lesion on the penis, I should suggest a diagnosis of balanitis xerotica obliterans closely allied if not identical with lichen sclerosus et atrophicus. One patient who had involvement of the prepuce, forming a constricting band encircling the penis, interfering with erection and making intercourse impossible, had much symptomatic relief with local injections of hydrocortisone suspension. Recurrence of symptoms after six months necessitated retreatment, with again relief of symptoms.

DR. STEPHEN ROTHMAN: Lesions of lichen sclerosus et atrophicus often arise at sites of previous trauma. In Dr. Spencer's case, amputation of the penis was followed much later by appearance of the lesion in the surgical scar. I have shown lesions of this disease developing in surgical scars. Dr. Brian Potter in our department has advanced the theory that lichen sclerosis et atrophicus represents an isomorphic (Koebner) effect in response to trauma.

Lymphosarcoma. Presented by DR. SAMUEL M. BLUEFARB, DR. SILAS WALLK, and (by invitation) DR. RICHARD I. BERNSTEIN.

A 65-year-old white man has lost 20 lb. during the past two months. Two weeks ago internal pruritus developed. There is no history of the recent ingestion of drugs or any history of allergy. He was recently treated here for pediculosis. He now presents generalized hyperpigmentation and hypopigmentation, with "scratch marks" and small areas of excoriation. There is a painless cervical, axillary, inguinal, and supraclavicular lymphadenopathy. These lymph nodes are moderately enlarged, firm, and of a "rubbery" consistency. There are several matted nodes in the right axilla. Roentgenograms were negative, and examination of aspirated bone marrow revealed an increase in eosinophils, red to white blood cell ratio of 1:5, and an abundance of plasmacytes. All of these findings are compatible with a lymphomatous disease.

Significant laboratory studies revealed the following findings: Hemogram: hemoglobin was 45% on Aug. 23, 1958, 62% on Sept. 4, 1958, 70% on Sept. 16, 1958. White blood cell count, 29,000 per cubic millimeter on Aug. 23, 1958 and 30,000 on Sept. 16, 1958, with 62% lymphocytes; 30% polymorphonuclear cells, 2% band cells, 3% eosinophils, and 3% monocytes..

Reticulum-Cell Sarcoma. Presented by DR. SAMUEL M. BLUEFARB, DR. SILAS WALLK, and (by invitation) DR. RICHARD I. BERNSTEIN.

A 74-year-old Negro first noted a "mass" in the left supraclavicular region two years ago. A similar "mass" was noted in the upper right side of the chest one year ago. Both "masses" were round, "liver colored," moderately soft, and not pulsating. They have shown no tendency to ulcerate until recently. This occurred after the performance of biopsies and the institution of roentgenotherapy. He has lost a considerable amount of weight since the onset of this illness. There has been no pain associated with the present condition. These "masses" have progressed in size and at the present time are approximately 20 cm. in diameter and are elevated about 12.5 cm. above the surface of the skin. The liver is palpable about 4 fingerbreadths below the right costal margin. Roentgenograms revealed complete destruction of the left clavicle and destruction of the fifth rib on the right side. There is no lymphadenopathy.

Laboratory studies revealed the following findings: Hemogram: hemoglobin 63%, red blood cells 3,740,000, white blood cell count 8,200, with 58% polymorphonuclear cells, 17% lymphocytes, 14% monocytes, 6% eosinophils, and 3% basophils. Biochemical examinations: cephalin flocculation 4+, thymol turbidity 6.0 units (MacLagan), γ-globulin turbidity 7.56/100 cc., uric acid 8.8 mg/100 cc., phosphorus 5.1 mg/100 cc., total protein 9.3 mg/100 cc., albumin 2.1 gm/100 cc., globulin 7.2 gm/100 cc. Urinalysis: negative. Aspirated bone marrow: "nonspecific" picture.

Mycosis Fungoides. Presented (by invitation) by DR. RICHARD P. REINERTSON and DR. BRIAN POTTER.

A 38-year-old white housewife had no skin trouble until about 1955, when she noticed both pink and light-colored areas on the abdominal skin, accompanied by moderate generalized itching. The patient states that new lesions have gradually appeared and that none of the lesions have disappeared spontaneously.

For about six months the patient has had occasional episodes of diarrhea, consisting of up to five or six bowel movements in a day.

Physical examination: Over the trunk and extending downward over both hips is an asymmetrical eruption consisting of erythematous, rather poorly defined plaques, becoming confluent and separated by areas rather lightly pigmented. The plaques are not scaly, but some are slightly thickened.

Histological description of biopsy specimen from abdomen: The epidermis shows acanthosis only. In the papillary layer of the corium are polymorphous infiltrations of mononuclear cells. Some of these have formed multinucleated cells and the nuclei of some of the other reticulum cells are somewhat bizarre.

Histologic description of biopsy specimen from right anterior axilla: The epidermis is irregularly acanthotic and slightly edematous but has not been invaded. In the upper corium, however, there is a polymorphous infiltrate of several types of mononuclear cells. The largest of these reticulum cells shows pleomorphism of nuclei. Except at the edge of the section, the infiltrate is not associated with the epidermis. Although the lack of involvement of the epidermis is not typical, this type of infiltrate occurs in mycosis fungoides.

Discussion

DR. JOHN R. HASERICK, Cleveland: I am confused by the terminology in the first case at Cook County Hospital. Lymphosarcoma is the presenting diagnosis, yet there is clear evidence in the protocol of bone marrow and hematological changes, consistent with leukemia. Leukemia is a generalized disease and lymphosarcoma a local one. The generalized lesions of leukemia represent hyperplasia, whereas those of lymphosarcoma are true metastases. Until we know more about these entities, it would seem best to keep them separated.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I should agree with Dr. Bluefarb that mycosis fungoides d'emblée is already a reticulum sarcoma. Dr. Winkelmann, Dr. Starr, and I have been going over some 500 cases that were labeled histologically as definite mycosis fungoides or probable mycosis fungoides. We have not completed this study. There are a good many cases, however, in which the histologic picture was that of mycosis fungoides but in which the patient terminated as Hodgkin's disease, lymphosarcoma, or reticulum-cell sarcoma. On the other hand, employing the criterion that Oscar Gans taught of polymorphous infiltrate with pyknosis and karyorrhexis and microabscesses of Pautrier and involvement of the epidermis, we have some cases that cleared with the minimum amount of superficial roentgen therapy. Other cases have been confused with local or generalized neurodermatitis. Mycosis fungoides in its earliest phases is one of the most difficult conditions to diagnose histologically.

DR. SAMUEL M. BLUEFARB: The diagnosis of lymphosarcoma was made from the axillary lymph

node. Although this patient had a white blood cell count of 30,000 per cubic millimeter, all the cells were normal and there were no "leukemia" cells in the peripheral blood or bone marrow. However, since lymphosarcoma and lymphocytic leukemia are so closely related, perhaps one should not be too dogmatic regarding this differentiation. When the lymphosarcoma cells enter the peripheral blood stream, then a "leukemic" picture is present.

Our second case is a reticulum-cell lymphosarcoma and is shown because of the dramatic response to x-ray therapy.

Congenital Ichthyosiform Erythroderma (Pityriasis Rubra Pilaris?). Presented by Dr. Theodore Cornbleet, Dr. Sidney Barsky, and (by invitation) Dr. I. Gigli.

Since birth, the skin of a 5-year-old Negro girl has been extremely sensitive, even to slight irritation. When she was 6 months of age "scaling," which soon became generalized, appeared. There have been some periods of remission which her mother attributes to the ingestion of vitamins A and E. However, subsequent course of this therapy were of no benefit. There has been no evidence of a "seasonal" influence on the cutaneous lesions; topical medications have not benefited the condition. This child has one sister who had the "same skin condition," but the lesions cleared when she was 9 years of age.

Physical examination disclosed only ectropion of the lower eyelids and generalized dryness, harshness, and scaling of the skin. There is some "tautness" around the nose and the hair is dry and lusterless. The entire cutaneous surface resembles that of "fish skin." Clinical impression: congenital ichthyosiform erythroderma.

Psoriasis(?) Pityriasis Rubra Pilaris(?) in Siblings. Presented by Dr. Frederick J. Szymanski, Dr. Stefan Bielinski, and (by invitation) Dr. Roland S. Medansky.

The older child has had an eruption since infancy. It started on the cheeks, then developed on the elbows, forearms, and knees. She has had various ointments, x-ray therapy, and also vitamin A orally prior to entering our clinic in April, 1956.

Physical examination at that time revealed a markedly symmetric erythematous scaly eruption on the cheeks, ears, and the external surface of arms and legs. The patches and lesions are sharply defined. There is a dry silver-like scale on the lesions. There are neither scalp lesions nor nail changes, and there are no follicular lesions of the proximal phalanges. Urinalysis and blood cell count were within normal limits.

Family history reveals one aunt having dermatitis on the extensor surface of the elbows and all male members on the father's side having dry skin.

In June, 1956, the patches on her face and arms were unchanged. However, at this time she developed follicular plugging on the proximal phalanges of her index fingers.

Therapy consisted of 1 grain (65 mg.) of thyroid daily for several months, 25,000 to 50,000 units of vitamin A daily, and an ointment of 2% salicylic acid, 5% ammoniated mercury, and 1% crude coal tar in petrolatum.

She continued to improve and in May, 1957, again showed the typical follicular plugs on the dorsum of the proximal phalanges of her fingers. However, this subsided and in July, 1957, she again developed a recurrence of the patches on her arms and face which more closely resembled psoriasis.

The younger child first developed lesions on his cheeks at age 6 months, followed by involvement of the ears, arms, and legs. There is a marked symmetrical distribution of the lesion, which are sharply outlined yellowish-red in color covered with a fine scale. Follicular plugging of several fingers was questionable and when the patient was last seen he also began to develop a keratoderma of the palms and soles.

Both children were presented at the November, 1957, meeting of the Chicago Dermatological Society. Since then, they have been followed at monthly intervals and appeared to improve markedly on 1% salicylic acid and 1% ammoniated mercury in petrolatum. Over the past few months they appeared to respond fairly well to Alphosyl-lotion in addition to the aforementioned therapy.

Histopathological report (of older child): A biopsy was performed on a typical lesion from the left arm. Histologic sections stained with hematoxylin and eosin revealed a mild thickening of the stratum corneum associated with intermittent parakeratosis. The epidermis is acanthotic, and the rete pegs extend downward to a horizontal line. The rete pegs are rounded at their inferior borders. The suprapapillary rete is thin in certain portions of the sections. A few round cells are seen infiltrating the epidermis, suggesting a Munro abscess. The changes are consistent with a diagnosis of psoriasis.

Congenital Ichthyosiform Erythroderma. Presented by Dr. H. J. Burstein, Decatur, Ill.

A girl aged 9 months has had since birth a generalized scaling eruption of face, trunk, and extremities. Her parents and three brothers, aged 5, 4, and 3 years, have had no similar eruptions. A first cousin supposedly died with a severe scaling eruption at 7 years of age. There is no other familial history of related skin disorders.

Examination reveals a normal infant except for a diffusely ichthyotic skin with areas of mild erythema. Flexural areas and palms are erupted. Nails and hair appear normal.

Serum proteins were 7.0 mg. %; albumin, 5.3 mg. %; globulin, 1.7 mg. %. Paper electrophoresis shows hypogammaglobulinemia, 6.3 % of total protein.

A biopsy specimen of lumbar region shows a thickened granular layer, vacuolated cells in epidermis, and vascular dilatation in corium.

Pityriasis Rubra Pilaris (Form Fruste?) in Father and Son (Reputed to be also in Grandmother and Brother). Presented by DR. W. N. SLINGER, Rockford, Ill.

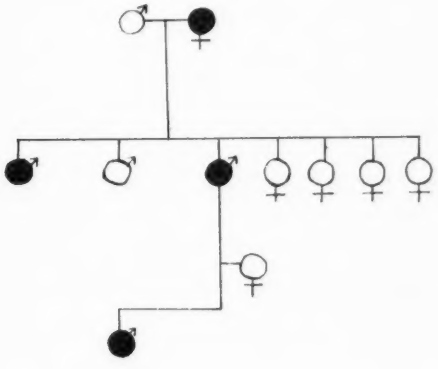
The father, aged 27 years, gives a history of having a finely scaling erythematous rash since the age of 14 years. The eruption began on the hands and has remained severest in this area. For the past 10 years, the eruption has been more or less generalized. Nail involvement developed during the past several years. The skin has cleared nearly completely without treatment several times some years ago. During the past three years of observation, he has nearly cleared twice while taking large daily doses of vitamin A (200,000 units). Repeated scrapings for wet mounts and cultures have been completely negative.

The son was first seen two years ago at the age of 2½ years. He has improved with the use of hydrocortisone and tar ointments and vitamin A by mouth. The eruption began on the dorsum of the toes. All smears and cultures have been negative. Patch tests to shoe material, chrome, and nickel were negative.

The schematic drawing shows the relative position of the father, brother, son, and grandmother.

Discussion

DR. STEPHEN ROTHMAN: In the case presented by Drs. Cornbleet and Barsky the patient displays ectropion and there is absence of the eyebrows. The disease has been present since birth. These and all other features fit the diagnosis of congenital ichthyosiform erythroderma.



DR. BLUEFARB: Is it the feeling at the Mayo Clinic that these children with pityriasis rubra pilaris eventuate into psoriasis?

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I do not think so. We have followed these so-called borderline cases and have done multiple biopsies and also carried out therapeutic tests. The differential diagnosis at times may be very difficult.

DR. FREDERICK J. SZYMANSKI: We had difficulty differentiating psoriasis from pityriasis rubra pilaris in our case. Histologically, it is a typical psoriasis; clinically the eruption is a typical pityriasis rubra pilaris.

I should like to say a word about Dr. Burstein's case that is labeled congenital ichthyosiform erythroderma. I should like to support this diagnosis because the histologic sections showed a granular layer which is characteristic of congenital ichthyosiform erythroderma, whereas in ichthyosis vulgaris the granular layer is absent.

DR. H. J. BURSTEIN, Decatur, Ill.: The protein-bound iodine is at the low normal, and response to thyroid should be of interest. Approximately 0.5% in a series of 2,000 various dermatoses reported by Hasselman and Schneider (University of Erlangen) showed hypogammaglobulinemia on electrophoretic examination. This disorder may represent a congenital biochemical as well as a cutaneous defect.

Eccrine Poroma. Presented by DR. SAMUEL M. BLUEFARB, DR. SILAS WALLK, and (by invitation) DR. CHESTER L. KROLL.

This 72-year-old white man first noted a red tumor, about 2.0 cm. in size, on the lateral aspect of the left foot, three years previously. About four months ago, there was an episode of bleeding from the tumor. He has not noted pruritus, "burning," pain, or "tingling," and the size and configuration of the lesion have not changed.

On examination there is a single, irregular, circumscribed, elevated red tumor on the lateral aspect of the left foot.

Discussion

DR. F. J. SZYMANSKI: Eccrine poroma is a name given to a rare tumor recently described by Hermann Pinkus. The few we have seen have occurred on the foot. Clinically, they are mistaken for pigmented nevi, or granuloma pyogenicum. Microscopically, they resemble a seborrheic keratosis, consisting of an epidermal tumor with a retiform appearance. There are, however, a few points of differentiation. First, keratin cysts are absent. Secondly, the essential cells forming the tumor are not basal cells. Actually, they are larger and paler than basal cells and they look like sweat gland cells. The overlying epidermis also differs from the major portion of the eccrine poroma,

whereas in seborrheic keratosis there is no difference between the superficial and the deep portions. Dr. Pinkus believes these tumors are derived from the superficial portion of the sweat duct. The eccrine poromas are benign tumors, and simple excision should be a satisfactory treatment. I am willing to accept this case as a good example of eccrine poroma.

DR. DAVID W. KERSTING, Milwaukee: Last week at Marquette we observed a superficial dark-brown sessile tumor on the sole of the foot of an elderly man, which had been present for 12 years. It was identical in all respects to the one so well presented here today, and we identified it with the name given this lesion by Dr. Pinkus—eccrine poroma. However, I think we must not fail to recognize that these tumors still represent one of the forms of basal-cell epithelioma, a sudoriferous type, if you will. The examples illustrated by Knox and Spiller in the ARCHIVES last June (A. M. A. ARCH. DERMAT. 77:726-729, 1958) confirm this. The eccrine poroma type is also illustrated in some of Krompecher's works on the "basalioma" and quite recently also by Smith and Coburn (*Brit. J. Dermat.* 68:400-418, 1956) under another name—"benign hidroacanthoma simplex." All are concerned with the sudoriferous element in these tumors.

DR. SAMUEL M. BLUEFARB: Clinically, the lesion in our patient resembled a granuloma pyogenicum. KNOX, in the A. M. A. ARCH. DERMAT. (77:726, 1958), called attention to the cup-shaped epidermal invagination from which the tumor protrudes. The increased vascularity of the tumor is a striking feature.

Papulonecrotic Tuberculid. Presented by DR. ALLAN L. LORINCZ and (by invitation) DR. RICHARD P. REINERTSON.

A 36-year-old white housewife had no skin trouble until 1955, when she first noticed lesions on the right extensor forearm. Lesions have since appeared on the extensor forearms, knees, and back. The lesions begin as red papules and nodules up to 1 cm. in diameter, become necrotic and crusted centrally, and heal with scarring after six to eight weeks.

The patient was born in Poland, was in a concentration camp during World War II, and came to the United States in 1949. There is no personal or family history of tuberculosis, and the patient's husband and two children have negative tuberculin test and chest microfilm.

On physical examination, the patient has lesions of the extensor forearms, knee, back, and scalp consisting of erythematous papules and nodules 3 to 10 mm. in diameter, which become centrally necrotic and crusted and heal with scarring.

Skin tests: P. P. D. No. 1 (equivalent to old tuberculin 1:10,000): 2.0 cm. erythema and induration. P. P. D. No. 1 diluted 1:100: negative. Old tuberculin 1:10,000,000: 2.0 cm. erythema and induration.

Course: The patient was started on isoniazid, 300 mg. daily, on Sept. 9, 1958. On Sept. 30, there had been no new lesions; however, on Oct. 8, the patient reported a new lesion on one hand.

Histological description of biopsy specimen of skin of left forearm: There is necrosis of the central corium and overlying epidermis. The viable corium is infiltrated with inflammatory cells, and in the center of some of these collections an inflamed blood vessel can be discerned.

Diagnosis: infarct compatible with papulonecrotic tuberculid.

Discussion

DR. ALLAN LORINCZ: To support a diagnosis of tuberculid one should be able to demonstrate a high degree of sensitivity to tuberculin. The chief point this case brings out is that skin testing for this purpose should be done with old tuberculin, rather than P. P. D. The reactivity to P. P. D. in this patient was no greater than might be expected in the overwhelming majority of adult persons. Her reactivity, however, to old tuberculin in greater than millionfold dilution is a finding which strongly supports the clinical diagnosis of tuberculid.

Bullous Lupus Erythematosus of the Scalp. Presented (by invitation) by DR. WILLIAM H. GILLESPIE.

A 46-year-old Negro woman first noticed blisters on her scalp in 1945 and has suffered from this disorder ever since. The blisters usually appear about two days before the onset of each menses and are preceded by pruritus of the scalp. After three or four days, the blisters dry up and then only the asymptomatic bald patches are noticed. She was first seen at the University of Chicago Clinics in August, 1958, and has been receiving chloroquine, 250 mg. b.i.d., during the past six weeks with subjective and objective improvement.

Examination of the scalp revealed two involved areas in the "part-lines" on each side of the vertex measuring 7×3 cm. The lesions were depigmented and atrophic in the center with only minimal peripheral erythema. One bulla measuring 1×2.5 cm. was observed at the anterior margin of the lesion on the left. A smaller bulla containing clear fluid was presented on the right side.

Laboratory data: blood sedimentation rate was 9 mm.

Biopsies: Biopsy specimen from the edge of a bulla shows liquefaction degeneration of the basal layer, with formation of a subepidermal bulla extending intraepidermally and roofed by layers of parakeratosis. In the corium there is a diffuse infiltration of inflammatory cells in which eosinophils are almost as numerous as lymphocytes. Histo-

logically, an atrophic lesion of the scalp shows moderate acanthosis and parakeratosis. The corium contains an infiltrate chiefly of lymphocytes associated in one instance with an adnexal structure.

Case for Diagnosis (Bullous Disease of the Scalp: Lupus Erythematosus? Pemphigoid?). Presented (by invitation) by DR. WILLIAM H. GILLESPIE and DR. BRIAN POTTER.

A 70-year-old retired male garment presser has had a blistering eruption of the scalp since November, 1956. The eruption has been moderately pruritic and has persisted with little change until the present time. He was first seen at the University of Chicago Clinics in April, 1957, and was started on chloroquine therapy. There was improvement, but the medication had to be discontinued owing to gastrointestinal symptoms.

In November, 1957, he was given Fowler's solution, and he continued this therapy until March, 1958, without remarkable change in the scalp. In early September, 1958, the patient was started on sulfapyridine, 0.5 gm. q. i. d., and has continued that regimen until the present time with objective improvement.

Examination of the bald vertex of the scalp revealed patchy involvement and erosions and bullae, the latter varying in size from 1-2 cm. There were patchy areas of erythema, scaling, and atrophy. Nonbullous erythematous lesions were also present on the posterolateral aspects of the neck.

Biopsy: Three biopsy specimens are presented. In two, there is a complete separation of the epidermis from the corium with hemorrhage and a tendency to the same in the third. Two of the sections show a marked parakeratosis. In all specimens there is moderate diffuse infiltration of the corium chiefly by lymphocytes. In the biopsy from a nonbullous lesion there is an area of necrosis of the epidermis and upper corium.

Discussion

DR. MARCUS R. CARO: I was particularly interested in Case 5. I agree that the patient has at the present time atrophy of the scalp with findings which are not consistent with a diagnosis of lupus erythematosus. The section showed a considerable amount of parakeratosis and moderate acanthosis, and these two features are not seen in bullous lupus erythematosus.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I agree with what Dr. Caro said about the first case. The second case would fit in with what Dr. Brunsting has described as benign pemphigoid in a paper recently published in the ARCHIVES, April, 1957.

DR. SILAS WALLK: I am interested in the discussion on the second case because at Cook County Hospital about three years ago we had a case which was labeled as pemphigoid. We followed him for three years, and he finally developed leukemia.

DR. CARO: Dr. Wallk mentioned a point which we often overlook, but, which is important, that in old persons you may have bullae in dermatoses which are not ordinarily bullous in the young.

DR. J. M. MCCUSKEY, Peoria, Ill.: I should like to ask Dr. Montgomery if he knows what Dr. Brunsting's experience has been with the steroid preparations, especially the newer ones, in these pemphigoid eruptions. Some of the bullous eruptions that are or may be related to pemphigus vulgaris have not responded well to the older preparations but have sometimes done well with the new ones.

In March, 1956, I presented two cases of pemphigus erythematoides before this Society. Neither of them was appreciably benefited by cortisone, hydrocortisone, or prednisolone given for a long time in fairly large doses. However, both patients have responded remarkably well to one of the triamcinolone preparations. It has been possible to keep them relatively free of lesions by giving from 4 mg. to 8 mg. daily.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I cannot answer the question raised by Dr. McCuskey in regard to steroid therapy and of Dr. Brunsting's cases of benign pemphigus. He had a rather marked eosinophilia and was eventually found to be allergic to certain foods; has remained free from lesions since eliminating these foods from his diet.

Adenoma Sebaceum (Tuberous Sclerosis). Presented by DR. W. N. SLINGER, Rockford, Ill.

This 9-year-old boy first exhibited nevoid lesions of the face at 10 months of age. These first lesions were described as small pigmented spots which slowly increased in size. The papular paranasal lesions developed later. In recent months new roughened, pigmented lesions have been developing in the scalp.

Epileptiform seizures began three and one-half months after birth. There were frequent attacks until the 17th month, when successful control was established with anticonvulsants. Medication was discontinued at 4½ years of age, and there has been no recurrence of the seizures.

Asthmatic attacks began at the age of 7 months. These have continued, in spite of the ministrations of an allergist. Recently, episodes of asthma have become increasingly infrequent.

School history has been complicated. Tests taken on admission to the first grade of a private school at age 5½ years demonstrated a bright-normal level of verbal understanding but a marked delay in visuomotor ability in drawing, and a lack of established preference for either hand. Attempts

at education both at private and public schools were unsuccessful. He is now receiving schooling at home from a private teacher.

Electroencephalograms were taken several times and reported "clear." However, the psychometrist was of the opinion after extensive psychological testing that the results of the tests strongly indicated a marked exogenous handicap referable to the cerebrum or diencephalon, superimposed on well-endowed mental brightness.

All the general physical examinations by a pediatrician and repeated laboratory examinations have been within normal limits.

Discussion

DR. OTTO STEGMAIER, Davenport, Iowa: This boy presented a patch of pigmented skin on the left cheek in addition to the epilepsy and suggestive mental deficiency. He did not have the nail ridges associated with subungual fibromata. There may be tumors of the kidney or of other organs associated with tuberous sclerosis. A 15-year-old girl whom I recently saw had no other manifestations of this ensemble except adenoma sebaceum; she died of a brain tumor.

DR. J. M. MCCUSKEY, Peoria, Ill.: The triad of mental deficiency, epilepsy, and skin tumors which have been called epiloia are described by Butterworth and Wilson (*Arch. Dermat. & Syph.* 43:41 (Jan.) 1941). Any member of the triad may be present or there may be various combinations of these and one or more of a great many cutaneous and visceral anomalies. Some of the cutaneous anomalies are hyperpigmented or depigmented areas, various sized tumors, especially in the scalp, pigskin-like lesions on the trunk, subungual fibromas and many others. Usually, it is possible to obtain a history of one or more of these cutaneous or visceral abnormalities or insanity in other members of the family. One of the patient's grandmothers was confined to a mental institution and a further search might reveal other manifestations of epiloia.

DR. STEGMAIER: According to Wilson and Bruce, epiloia is a pseudo-Greek verbal artifact coined by Sherlock, in 1911. He favored the term because it was meaningless, short, and easily capable of forming an adjective.

DR. W. N. SLINGER, Rockford, Ill.: I dislike adding to the profusion of names, but I believe pediatricians, ophthalmologists, and other groups know this syndrome as Bourneville's disease. Retinal nodules are described as a common finding by ophthalmologists. Such lesions are, therefore, a distinct aid to diagnosis. This patient has a nodule of this type in the right retina.

Blastomycosis. Presented by DR. IRENE NEUHAUSER and DR. ROLAND S. MEDANSKY (by invitation).

This 46-year-old Negro male Arkansas-born farmer was well until 1953, when he began to notice progressive shortness of breath, which apparently became so severe that a tracheotomy was done. He was then transferred to a tuberculosis sanatorium in Arkansas, where he was treated with intramuscular streptomycin for six months and pills for his two and one-half years of hospitalization. The patient does not know whether his sputum is positive, but he was told that he had tuberculosis of the "bronchial tubes." His dyspnea improved but he still has some difficulty with breathing on exertion. He has residual hoarseness. When he left the tuberculosis hospital, he still had a dressing on his neck, and when the tape and dressing were removed he noticed a papule on the left side of his neck which eventually broke down, ulcerated, and spread down along the side of the neck, increasing in size very slowly over the past two years. He has been on no medication.

On physical examination the essential findings are as follows:

1. The skin shows an ulceration on the left lateral and anterior side of the neck extending to the right side of the neck, with irregular borders of a violaceous hue, a sharp sloping border, and tiny pustules along several margins.

2. The ear, nose, and throat examination reveals bilateral fixed vocal cords of scarred tissue. No active process at this time.

3. There is no prostatic enlargement; normal consistency with slight tenderness of the left lobe.

4. The chest shows decreased expansion with decreased breath sounds. No rales or dullness. Respiration slightly labored with exertion, and wheezes in the laryngeal area.

Laboratory examinations: Chest x-ray shows scarring and retraction of the right upper lobe involving primarily the apical and posterior segments, which is compatible with tuberculosis.

Second-strength P. P. D. was positive in 48-72 hours. Blastomycin, coccidioidin, and histoplasmin skin tests were all negative in 48 hours. Blastomycosis complement-fixation tests positive in 1:32 dilution. Blastomyces dermatiditis positive on direct smear and culture. Cultures in progress for prostatic and bronchial secretions.

Histopathological report revealed a thick scale crust on an acanthotic epidermis. The infiltrate consists of numerous polymorphonuclear leukocytes, plasma cells, histiocytes, and giant cells. Doubly refractile and thick wall organisms resembling blastomyces are located within the crusted zone and upper corium.

Therapy: Patient was started on amphotericin B (Fungizone) on Oct. 7, 1958. To date he has re-

ceived 225 mg. in divided doses, and there appears to be a slight improvement. Amphotericin B was started on this patient in the dosage of 0.25 mg. per kilogram per day and will gradually be increased to the maximum dosage of 1.0 mg. per kilogram per day.

Discussion

DR. LEON GOLDMAN, Cincinnati, Ohio: This is a very important case because it illustrates an old dictum about granulomas. You can argue as much as you wish about specific characteristics of the diagnosis of a granuloma, but, unless you can demonstrate the causative agent, you can never be certain as to the diagnosis. I wonder how much active blastomycosis, especially the pulmonary type, is still present. As you know, formerly blastomycosis was a national disease, blastomycosis was considered as a primary cutaneous reaction.

How do we evaluate the response to therapy in regard to fibrotic pulmonary lesions? The skin lesions are easier to follow than the deep pulmonary foci. We have learned recently that the pulmonary function unit of a modern hospital set-up is a good place to follow the improvement of the pulmonary focus in systematic mycoses. From my personal experience, I do not know how long a patient should be kept on amphotericin. We initiate therapy with intravenous amphotericin B, and then try to hold on oral capsules for the maintenance of therapy.

The duration of therapy depends upon the response and also the reactions. If the dosage is built up slowly, then we are less likely to run into serious reactions. The reactions that have been disturbing have been those of renal involvement and of the blood. The chills and fever types of reactions are uncomfortable but not serious. Amphotericin B is the preferred treatment for blastomycosis now.

DR. IRENE NEUHAUSER: I wish to cite a case of generalized moniliasis which we have been following for years at the University of Illinois. We tried many types of medication without any beneficial results. Recently, the patient was given amphotericin B and cleared completely. It is too early to evaluate the results of the treatment of the deep mycoses with amphotericin B, but in this case the treatment was certainly effective.

Scleroderma. Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and (by invitation) DR. JOSE LATONI.

Dermatomyositis. Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and (by invitation) DR. CHESTER L. KROLL.

Necrobiosis Lipoidica Diabeticorum. Presented by DR. DAVID V. OMENS, and (by invitation) DR. HAROLD D. OMENS and DR. RICHARD I. BERNSTEIN.

Sarcoidosis with Granulomatous Uveitis. Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and (by invitation) DR. JOSE LATONI.

Sarcoidosis. Presented by DR. SAMUEL M. BLUEFARB and (by invitation) DR. FRANK DUNLAP and DR. J. HASEGAWA.

Arteriovenous Aneurysm. Presented by DR. SAMUEL M. BLUEFARB, DR. SILAS WALLK, and (by invitation) DR. RICHARD I. BERNSTEIN.

Bowen's Disease. Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS and DR. JOSE LATONI.

Senile Keratoses with Bowenoid-like Changes. Presented by DR. ARTHUR L. SHAPIRO.

Basal-Cell Epithelioma. Presented by DR. A. M. BUCHHOLZ.

Annular Lichen Planus. Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS and DR. RICHARD I. BERNSTEIN.

Lichen Striatus. Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS and DR. JOSE LATONI.

Case for Diagnosis. Presented by DR. HAROLD SHELLOW and (by invitation) DR. ROLAND S. MEDANSKY.

Case for Diagnosis. Presented by DR. JULIUS E. GINSBERG and (by invitation) DR. CHRISTINE SUTTON.

Incipient Acrodermatitis Chronica Atrophicans. Presented by DR. ARTHUR W. STILLIANS.

Extensive Superficial Hemangioma Associated with Anomalies of the Deep Vessels. Presented by DR. ALBERT H. SLEPYAN and (by invitation) DR. BETSY B. BRENNAN.

Case for Diagnosis (Localized Pathergic Granuloma). Presented (by invitation) by DR. ROGER W. PEARSON, DR. ARNOLD A. COMBINER, and DR. BRIAN POTTER.

MANHATTAN DERMATOLOGICAL SOCIETY

Perry Sachs, M.D., President
Maurice J. Costello, M.D., Secretary

Nov. 11, 1958

Gangrene of Skin From Meningococcemia. Presented by DR. J. HARRY KATZ.

A man aged 32 developed meningococcemia about eight weeks ago. There was high fever, severe malaise, and hemorrhages throughout the skin, particularly on the thighs, where they were severe. When convalescence began, about three weeks ago, large crusts formed at the sites of the hemorrhages. Some of the smaller crusts have disappeared, leaving pitted scars.

Scattered, round, pitted scars with depressed centers are seen on the trunk and extremities.

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On the anterior aspect of the thighs are large trough-like ulcerations, some still filled with crusts, others with a purulent exudate.

Treatment has consisted of Chymar, 0.5 cc. twice weekly, Varidase buccal tablets, and neomycin ointment locally.

The hemoglobin level, white blood cell counts, and differential counts are within normal limits, as is the urinalysis.

Discussion

DR. JACK WOLF: This is a very interesting eruption, one we certainly do not see often. Such extensive destruction must surely be an uncommon accompaniment of the Friderichsen-Waterhouse syndrome, even when extensive hemorrhage occurs. Simple topical therapy is all that is required, but healing will be associated with considerable scarring.

DR. MAURICE J. COSTELLO: It is the most unusual eruption I have ever seen. I discussed a paper by Hill, of Boston, at the American Medical Association convention in San Francisco, and he listed about 10 different types of eruptions that may be associated with meningococcemia. I would gather that this man was heading for the Friderichsen-Waterhouse syndrome. I think one may forestall formation of keloids by giving massive doses of antibiotics, especially penicillin.

DR. JOHN W. DOUGHERTY: Enzyme treatment does not seem to make much sense when you consider that the blood stream is filled with enzyme inhibitors. However, the patient says that since he started on enzymes he has improved more in a week than in the three weeks previously.

DR. WILBERT SACHS: Years ago we used to call this sphaceloderma, and any sphaceloderma based on systemic infection was called ecthyma. This might not have been due to the meningococcus. We saw that years ago, but not so much now.

DR. PERRY SACHS: During the war we saw a large series of patients with meningococcemia, and all showed various degrees of purpura and hemorrhage, but we never saw the amount of hemorrhage that this patient shows, nor did any go on to ulceration.

DR. JULES VANDOW: I have seen children with Friderichsen-Waterhouse syndrome, and they all died, but that was before the advent of the steroids. Now they can be kept alive with steroid therapy.

DR. DAVID BLOOM: The gangrenous ulcers in this patient I am inclined to consider as pyoderma gangrenosum. The γ-globulin content of the serum should be determined. Even if it is not too low, it should be administered together with other supportive therapy, including steroids.

DR. MAURICE J. COSTELLO: The organism has been demonstrated in some cases of chronic meningococcemia, and I wonder whether it was found in this patient.

DR. J. HARRY KATZ: I gave only a small dose of Chymar until the patient was presented tonight. We will take a culture of the exudate. When he first came in there was hardly any exudate; the troughs were entirely filled with clots. I suspected there might be some exudate under the crusts.

DR. MAURICE J. COSTELLO: I think Dr. Vandow's explanation is the proper one. This man might have died if he had not received steroids.

DR. WILBERT SACHS: Slides in meningococcemia show tremendous toxicity, with sandering connective cells. It is surprising to me that any skin involved by the meningococcus does not have tremendous hemorrhages because of the great amount of toxicity.

A Case for Diagnosis (Erythema Nodosum?)

Presented by DR. J. HARRY KATZ.

A woman aged 43 first noted a rash on the back of her left leg 15 years ago. It lasted about a year and then disappeared. In February, 1952, a new lesion appeared on the anterior surface of her left leg, and similar lesions have appeared and disappeared more or less regularly since, each leaving a depressed scar. She now presents a new lesion, which developed a few days ago. The lesions are tender and remain so until they disappear. They respond well to low doses of steroids.

There are scattered brownish areas on the lower part of the left leg, with scarring in some of the lesions. There is also a tender purplish lesion about 1 cm. in diameter on the anterior surface of the left leg. The lesion is slightly raised and tender.

Biopsy findings were reported as (1) nonspecific chronic inflammation and (2) chronic granuloma.

Urinalysis was normal, and a roentgenogram of the chest was not remarkable. Serologic tests for syphilis and tuberculin tests in dilutions to 1:100 were negative. Mycological examination of the toenails was positive for fungi, but examination of the glabrous skin of the feet was negative. The erythrocyte sedimentation rate was 2 mm. in one hour. The glucose-tolerance test was normal, and a cryoglobulin study in 1956 was negative.

Discussion

DR. MAURICE J. COSTELLO: I think the lesions are due to Trichophyton rubrum. It is a unilateral folliculonodular process simulating papulonecrotic tuberculid. I cured my patients with Anthralan. It may last for years if untreated. The eruption may be unilateral.

DR. JOHN W. DOUGHERTY: These patients are usually brunettes, and they are more likely to shave their legs than blondes. I think part of the therapy is manual epilation of hairs.

DR. GEORGE M. LEWIS: These lesions are a little large for T. rubrum folliculitis, but that is possible.

DR. J. HARRY KATZ: In Wilson's cases, were not more follicles involved? This girl has had only one involved at a time. It appears as a tender, soft area.

DR. M. J. COSTELLO: The lesions may occur in groups and may be one or two or many. She has new pustules and old lesions undergoing involution. When you get one of these patients well they are really happy. I think these eruptions do not get well because they are not recognized as a fungous infection.

A Case for Diagnosis (Lymphoma Cutis? Parapsoriasis?). Presented by DR. J. HARRY KATZ.

A Case for Diagnosis (Pityriasis Rubra Pilaris? Lichen Planopilaris? Keratosis Pilaris?). Presented by DR. J. HARRY KATZ.

A Case for Diagnosis (Pustular Psoriasis?). Presented by DR. JACK WOLF.

A Case for Diagnosis (Insect Bites? Dermatitis Herpetiformis?). Presented by DR. J. HARRY KATZ.

A Case for Diagnosis (Keratosis? Lichen Planus?). Presented by DR. THOMAS N. GRAHAM.

NEW ENGLAND DERMATOLOGICAL SOCIETY

Joseph Goodman, M.D., President
William R. Hill, M.D., Secretary

Oct. 12, 1958

Cutis Laxa (Dermatomegaly). Presented by DR. FRANCESCO RONCHESE.

A boy aged 2 years, the child of a physician, has been noted to have loosely folded skin since birth. His physical and mental development have been otherwise normal. He is presented for suggestions as to therapy and for guidance in prognosis.

Discussion

DR. FRANCESCO RONCHESE: I first saw the child when he was six months old. He then had more subcutaneous fat, and the skin did not hang in folds as much as it does now. With a diminution of subcutaneous fat one can expect an accentuation of symptoms. Only three cases of this congenital disorder have been reported in the literature, and this one will make the fourth. None of the three reported was seen after infancy (see discussion of paper of Robinson and Ellis: A. M. A. ARCH. DERMAT. 77:665, 1958). Consequently, to my knowledge, no one can speak from experience concerning prognosis or treatment. Cutis laxa is a lax term, in my opinion, improperly used as synonymous with cutis hyperelastica, Ehlers-Danlos syndrome, the pendulous tumors of von Recklinghausen's disease, etc. Cutis laxa, for which I proposed the term dermatomegaly, is simply a disorder of excess, in which there is more skin than body surface to cover. The skin consequently hangs in folds like that of the bloodhound. It is not related to cutis hyperelastica, Ehlers-Danlos syndrome, etc. I am happy that Dr. Conway suggested a plastic face lifting. The child will soon go to school, and we should try to improve his facial appearance. The body is of secondary importance. As far as I know, this would be the first case of cutis laxa to have a face-lifting operation. As in any surgical procedure, we may get keloidal or retracted scars, but it is worth the chance. If the facial appearance would be corrected, it would be a great step forward.

DR. HERBERT MESCON: We have working in our department a Ph.D. candidate in the Department of Biochemistry, who is analyzing skin chemically in regard to collagen changes, both in age and in diseases such as this, pseudoxanthoma elastica, and Ehlers-Danlos syndrome. We should like to study material from patients who have these relatively rare diseases. A formalin-fixed biopsy specimen can be used, but a small frozen biopsy specimen is preferred. We should be glad to travel to obtain such a specimen and to transport it in Dry Ice.

DR. MAURICE M. TOLMAN: This is truly a congenital defect. Whether it is a functional congenital defect as opposed to a structural defect is the basic question.

DR. HERBERT MESCON: We do not know the answer to this. Certainly in many of this group of diseases, collagen is one of the organs affected. The more we know about the changes in the chemistry of collagen, the more chance we may have of getting at basic changes. I do not know the cause.

Total Alopecia and Vitiligo. Presented by DR. AARON B. LERNER.

A man aged 41 years noted pruritus of his scalp, erythema, and minimal hair loss about 18 months ago. At the same time an erythematous eruption appeared on his chest. This became increasingly severe and prompted his admission to

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Massachusetts General Hospital, where 10 days of exhausive investigation failed to disclose a diagnosis. Loss of hair continued and within the next few months the body hair, eyelashes, and eyebrows disappeared. In addition, his skin, which had been dark and tanned, became very fair and burned readily on exposure to sunlight.

There is no family history of vitiligo or alopecia. The patient feels he has been in excellent health and under no stressful situation. During the war, he was troubled by ulcerative colitis, but this has been fairly quiescent in recent years with no exacerbation prior to the time he was first seen in the dermatology clinic. In the past few months, however, there was an episode of renal colic and a flaring of his ulcerative colitis.

On physical examination the patient was in fairly good general health. Certain serologic studies were carried out: blood pepsin was evaluated at 420 units, which is within normal range, but serum butyl-extractable iodine was 11.7μg. %, which is elevated but unexplained. The patient has none of the common symptoms of thyroid dysfunction. A repeated examination gave even higher values—15.7μg. %, but the radioactive iodine uptake was well within the euthyroid range. The total cholesterol was 249, which is within the normal range of 123 to 274. Total fatty acids were somewhat elevated at 20.4. Lipid phosphorus was normal—10.7. The 17-ketosteroids were 2.4 mg. in 24 hours, and the ketogenic steroids were 2.4 mg. in 24 hours. A corticotropin (ACTH) test gave a preinjection value of 29.2μg. per 100 cc. and a postinjection value of 43.7μg. per 100 cc.

Early in May, the patient was started on Tolseram, 3 gm. per day, for about three weeks. He complained bitterly of fatigue and irritability, and the drug was discontinued. In recent months there has been considerable regrowth of white hairs over the chest and about the bearded area, so that the patient again has to shave.

Discussion

DR. CHARLES SHEARD: I have three patients with alopecia totalis, all of them growing hair and all of whom have been found to be suffering from mild emotional strain which could not be elicited in an ordinary way by a dermatologist.

DR. HARVEY B. ANSELL: I was much interested in a positive finding in alopecia areata and wonder whether Dr. Lerner will comment on it. It is the first positive report, to my knowledge.

DR. AARON B. LERNER: We do not know the reason for the relatively low output of 17-ketosteroids in the urine. Also, we have not been able to account for the markedly elevated blood iodine as determined by measuring the butanol-extractible iodine in the blood. He has one of the highest blood iodine values that we have seen. We questioned him repeatedly as to whether he had had any iodine compounds injected for x-ray studies. As far as we know, he has never received iodides. In spite of the high blood iodine level, the radioactive iodine uptake by the thyroid gland is normal. Clinically, he does not have hyperthyroidism. This patient developed total alopecia and total vitiligo almost simultaneously. We have two other patients with total alopecia and total vitiligo. A few months ago the patient being presented had no hair, but now a fair amount has regrown. All of the new hair is without pigment. Something happened to all the melanocytes in the body and to all the hair follicles to bring about a pronounced change. This change is reversible, because we know that persons receiving sufficient amounts of steroids will get regrowth of hair and that some of the hair will have pigment in it.

We have found that most patients with alopecia areata or totalis have increased output of the melanocyte-stimulating hormone, MSH, in the urine. We do not know the significance of this finding, but we attribute the alopecia to some hyperfunction of the pituitary gland.

DR. NEVILLE KIRSCH: Is there any explanation for the apparent looseness of the tissues? When you feel the bald areas of these people with alopecia areata, they seem to have loose skin and depressed areas that look like pseudoatrophy. The skin is flabby. Have any studies been done on the chemistry or physiology of this change in the cutis to explain it?

DR. ELLWOOD WEISE: As to Dr. Ansell's point about stress, I had occasion in New York a number of years ago to inquire carefully into the history of all patients coming into the clinic with alopecia areata presumed due to stress factors. By inquiring into the histories of other patients who came to the dermatological clinic for entirely unrelated conditions, we have found that the same history of stress could be obtained in an even greater degree than in those with alopecia areata.

DR. WALTER C. LOBITZ, JR.: In answer to Dr. Kirsch's question, we may be able to hypothesize the reason because it certainly is there clinically. I think all the hair follicles in areas of alopecia areata are in telogen. This is a resting stage, and why they all go in telogen at one time in one area on human skin is not known. Of course, it is common for certain animals to have waves of hair growth so that the hair in a given area is either in anagen, catagen, or telogen. In the animals that do this there is a definite relationship between the size of the dermis and the stage of growth of the hair follicle, so that the anatomist can pick up a rabbit or a rat and feel the texture of the skin and predict exactly what stage of growth

the hair follicle is in, whether growing in anagen or resting in telogen.

This might well be the very same in alopecia areata in the human being. Dr. Montagna's book, "The Structure and Function of Skin," reemphasizes that there is a tremendous interplay between all of the epidermal and the dermal structures. Until we understand the role of one toward the other we have a great deal of stumbling about to do. This may well be a good example of that.

DR. O. R. JOHNSON: I remember very well a young lady who on many occasions accompanied her father on hunting and fishing trips. She admitted that she idolized him but was not particularly fond of her mother. While on one of these trips her father died suddenly of heart disease. Inside of a month she lost all her hair, and in a year's time it was practically all back again. So in this case I feel that there is a definite psychological factor.

Total Vitiligo. Presented by DR. AARON B. LERNER.

A 41-year-old woman first noted vitiligo at the age of 14. It gradually progressed and became extensive. At the age of 37 the patient was found to have no thyroid abnormality and was considered a good candidate for total depigmentation. Her son, aged 10 years, has had vitiligo since the age of 8 and is undergoing repigmentation with the oxypsoralens.

The patient was depigmented with Benoquin ointment and uses a sun-screening agent during the summer.

Discussion

DR. NEVILLE KIRSCH: How do you distinguish the therapeutic effect of Benoquin from a normal spontaneous spreading of vitiligo over the entire skin surface? Do you mean that the normal pigmentation of the skin was removed by the Benoquin?

DR. JOHN E. LEDONNE: I notice this woman has been using sun-screening agents during the summer. If she did not do this but was exposed to the sun, what would happen to her skin? Would she get normal pigmentation or reappearance of the original vitiliginous lesions? Secondly, would you make a few comments on your experience with psoralen and its use in treatment of vitiligo in general?

DR. AARON B. LERNER: This patient has obtained such good depigmentation of the exposed parts of the body that it is difficult to see that she has a pigmentary defect. She was presented in one of the student practical examinations last year. None of the students or members of the resident staff realized that she had complete vitiligo of the exposed parts produced therapeutically. The monobenzoether of hydroquinine was responsible for the depigmentation, because she began treatment by using the ointment on one arm until it became depigmented, and subsequently she worked on the other arm.

From our limited experience with patients with extensive vitiligo who undergo therapeutic depigmentation, we find that they have little protection from sunlight. On exposure to the sun a perifollicular type of repigmentation often occurs. We instruct the patients not to expose themselves unnecessarily to the sunlight. The patients often apply a light protective ointment when they are going to be out in the sun for any period of time.

DR. HARRY SIGEL: Is it easier to depigment than to repigment?

DR. AARON B. LERNER: In general it is easier to depigment than to repigment a patient. The main difficulty with depigmentation is that about 15% of patients who apply monobenzoether of hydroquinone ointment become sensitive to the drug. When sensitization occurs, therapy becomes difficult.

DR. JOSEPH GOODMAN: Have you used Benoquin for patients with chloasma?

DR. AARON B. LERNER: Yes, but the results are only fair. About half the patients respond to therapy and some become sensitized to the drug. The results with this drug are not as good in the treatment of chloasma as they are in vitiligo.

Cryptococcosis Complicating Boeck's Sarcoid. Presented by DR. MARIE-LOUISE JOHNSON

A woman, aged 38 years, had a biopsy of a supraclavicular node 11 months ago, resulting in a diagnosis of Boeck's sarcoid. She was treated with Meticorten and was asymptomatic until late May, when her steroids were tapered off and she began to have headache. When admitted to the hospital in July of this year, she was found to have papilledema with an increase in cerebrospinal fluid pressure. There was a mild cellularity of the spinal fluid with an increase in protein and a decrease in sugar. Four specimens taken from successive lumbar punctures grew Cryptococcus neoformans on culture. At the time of the first admission a small (1 by 0.5 cm.) tan-pink, flat-topped, fleshy lesion was noted on the dorsum of the left hand. Biopsy proved it to be a cryptococcal lesion.

Despite intensive intravenous amphotericin therapy, which has controlled the central nervous system symptoms, there has been a regrowth of the granulomatous lesion in the site of biopsy from the left hand. In addition, a pink-brown, slightly raised eruption has been noted over the bridge of the nose and on the left leg.

Biopsy showed a dense, circumscribed, granulomatous reaction in the cutis with an overlying

thickening and bulging of a slightly hyperkeratotic epidermis. Numerous budding yeasts were present, both within and outside giant cells. Rarely was a capsule seen. In view of the clinical history and cultures, the impression was cryptococcosis of the skin of the hand.

Discussion

DR. FREDERICK REISS: As far as I can remember, this is the first case in which cryptococcosis has been associated with Boeck's sarcoid. Another remarkable point should be emphasized: Amphotericin B treatment has not the same effect on the cutaneous lesions as on the process in the central nervous system, which of course is well known.

Would not it be advisable to inject amphotericin B into these lesions? That has been accomplished successfully by Dr. Harber at Bellevue Hospital in a case of chromoblastomycosis.

I should like to ask Dr. Lerner whether any biopsy has been made from the lesion of the nose and whether this should also be considered a cutaneous manifestation of cryptococcosis. I doubt it very much because the lesion is rather flat, and I would not expect it to be a cryptococcosis of the skin. However, one never knows, because the cutaneous manifestations of cryptococcosis are so protean that one may get a surprise.

DR. JACK ALBOM: Three or four years ago I saw this patient and treated her for typical lesions of discoid lupus erythematosus. At that time she did not have any of the findings we see now. When discharged she had the little fine lesion on the nose that we see now. Biopsy at that time was refused, but there was an excellent response to Aralen therapy.

DR. AARON B. LERNER: As to whether this patient developed the cryptococcosis secondary to steroid therapy for sarcoidosis or had the infection before steroid therapy was begun, all we can say is that she manifested clinical cryptococcosis after steroids were used. She still needs steroid therapy for the sarcoidosis. In contrast to Dr. Reiss' experience, we have found in another patient with cryptococcosis that the clinical response to treatment with amphotericin was dependent solely on the dosage. When sufficient amounts were given, the lesions would clear.

I am hesitant to say what the lesion on the nose would look like microscopically. It could be an area of cryptococcosis infection. When we first saw the patient a small, soft, flat, yellowish papule was present on the arm and I did not think it represented an area of infection. However, a biopsy specimen revealed Cryptococcus neoformans in the tissue.

Systemic Cryptococcosis. Presented by DR. AARON B. LERNER.

A 65-year-old machinist developed skin lesions about three years ago. Those on the right elbow and chest are said to have followed trauma, but additional lesions behind the right ear and on the forehead and left arm seemed to be spontaneous. Initially, they appeared as small granulomas, but over a period of months they progressed to clearly defined, nonindurated ulcers. The lesion on the right elbow measured 5 by 5 cm. and that behind the right ear was larger. There were no systemic complications. The patient was previously presented at the Atlantic Dermatological Conference in 1958.

When the patient was first seen, two years ago, biopsies revealed a budding, yeast-like organism. Cultures of the biopsy material, which included a lymph node, and cultures from the sputum and urine yielded C. neoformans. All other physical findings and laboratory data have been normal except for a mildly elevated nonprotein nitrogen level, which occasionally rises with intensive amphotericin therapy.

In the past two years the patient's fungous infection has been kept under control with amphotericin B given parenterally. Initially and during periods of exacerbation the intravenous route is the only effective one and hospitalization is required. During the past summer after an intensive course of the intravenous medication with dramatic improvement in the lesions but not complete remission, the amphotericin was stopped and the patient was given 8-methoxypsoralen with exposure to sunlight. Clinically, the lesions have healed completely, and the patient seems better than at any previous observation.

Discussion

DR. FREDERICK REISS: I congratulate Dr. Lerner on this unusual therapeutic experience with 8-methoxypsoralen. I wonder how he would explain this therapeutic response. To me it is most unusual and very interesting.

DR. AARON B. LERNER: This person has been one of our star patients. Many of you saw him at the Atlantic Dermatological Society meeting in Boston. He has responded well to therapy with large amounts of amphotericin B intravenously. There was little improvement when it was given intramuscularly or orally.

While the patient's response to intravenous amphotericin therapy has been good, it is not an easy treatment. He has to be hospitalized to receive it, and he requires repeated courses of therapy. It is for this reason that we have been interested in finding some other approach to the treatment of his cutaneous and systemic cryptococcosis infection.

It is well known that the psoralens in conjunction with sunlight have a fairly general antibacterial and antifungal action. The patient made an excellent response to 8-methoxypsoralen and exposure to sunlight. No amphotericin had to be given during the summer months. The psoralens will be withheld this winter. We are interested to know whether the cryptococcosis will make itself evident again.

From the Floor: I should like Dr. Lerner to tell us whether this case of cryptococcosis has been cured, or only suppressed, with amphotericin.

DR. AARON B. LERNER: The infection in this patient has been suppressed, not cured. Fortunately, no one has shown that any of the fungi develop a resistance to amphotericin B, as do staphylococci to antibiotics. If we had a drug like amphotericin B that could be given orally, it might be possible to keep the patients on continuous treatment and thereby control the disease.

Addison's Disease with Vitiligo. Presented by DR. AARON B. LERNER.

Lupus Erythematosus Disseminatus. Presented by DR. MARIE-LOUISE JOHNSON.

A Case for Diagnosis (Lupus Erythematosus? Lichen Planus? Dyshidrotic Eczema?). Presented by DR. AARON B. LERNER.

Dermatomyositis. Presented by DR. MARIE-LOUISE JOHNSON.

A Case for Diagnosis (Lichen Nitidus? Lichen Planus [Koebner Phenomenon]?). Presented by DR. NEVILLE KIRSCH.

Dermatomyositis and Carcinoma of the Bladder. Presented by DR. AARON B. LERNER.

Fox-Fordyce Disease. Presented by DR. MARIE-LOUISE JOHNSON.

Mycosis Fungoides. Presented by DR. MARIE-LOUISE JOHNSON.

Primary Macular Atrophy of Schweninger-Buzzi. Presented by DR. CHARLES SHEARD. (Previously presented at the New York Academy of Medicine, October, 1951.)

A Case for Diagnosis (Pityriasis Rosea?). Presented by DR. MARIE-LOUISE JOHNSON.

Macular Atrophy. Presented by DR. CHARLES SHEARD.

A Case for Diagnosis (Congenital Ichthyosiform Erythroderma? Psoriasis?). Presented by DR. AARON B. LERNER.

A Case for Diagnosis (Pityriasis Rubra Pilaris Psoriasis?). Presented by DR. AARON B. LERNER.

Radiodermatitis. Scleroderma. Presented by DR. AARON B. LERNER.

Boeck's Sarcoid with Involvement of the Skin, Lungs, and Liver. Presented by DR. JACK ALBOM.

Scleroderma. Presented by DR. GUSTAVE SIROT.

Scleroderma, with Pigmentary Changes of the Hair Secondary to Chloroquine Therapy. Presented by DR. MARIE-LOUISE JOHNSON.

A Case for Diagnosis (Fixed Urticaria). Presented by DR. MARIE-LOUISE JOHNSON.

Keloids (Primarily Spontaneous). Presented by DR. CHARLES SHEARD.

Urticaria Pigmentosa with Systemic Lesions. Presented by DR. AARON B. LERNER.

Late Acne with Xanthelasma. Presented by DR. ALEXANDER TIMM.

NEW ENGLAND DERMATOLOGICAL SOCIETY

Nov. 19, 1958

Leukoplakia—Leukokeratosis. Presented by DR. FRANCESCO RONCHESE.

A white auto repairman, aged 65 years, has had lesions on his tongue for several years. He was hospitalized in 1946 for dizziness and ataxia, the diagnosis being encephalopathy due to carbon monoxide poisoning.

The patient shows white patches on the sides of the tongue and white, verrucous patches on top of the tongue of one year's duration.

After consultation at the Tumor Clinic of the Rhode Island Hospital, the consensus was that the patient had an epidermoid carcinoma of the tongue. Biopsy was recommended, with consideration of glossectomy if it proved confirmatory.

The blood Wassermann reaction was positive in 1955 and weakly positive in 1956. The microslide precipitation test was weakly reactive in 1958; Kolmer, reactive in 16 dilutions; Hinton, reactive in 1 dilution. Examination of the spinal fluid was normal. Biopsy showed no evidence of carcinoma.

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The patient received 6,000,000 units of penicillin in 1954-1955.

Leukokeratosis of the tongue.

The patient is presented for recommendations as to treatment.

Discussion

DR. WALTER F. LEVER: This patient has glossitis, most likely syphilitic. There are also patches of leukoplakia on the sides of his tongue. However, the lesions present on the dorsum of the tongue, extending to its tip and slightly beneath, are pedunculated, filiform, and, therefore, in my opinion, could well be verrucae vulgares. Of course, that is only a clinical impression and in order to verify it thorough histological studies would be necessary. I have not seen the slide, but there is a statement that carcinoma was not present. In many instances a diagnosis of verruca vulgaris can be made on histological examination. So, before any major procedure is undertaken, I suggest thorough histological studies.

DR. FRANCIS P. MCCARTHY: I disagree with Dr. Lever's suggestion that this process is verruca vulgaris. I regard this as a classic case of syphilitic glossitis, a condition that one rarely encounters today, as one expects to see it only in untreated syphilis.

This man has been a heavy smoker, and in the posterior third of the tongue the papillae are reasonably normal. The anterior two-thirds are completely bald with extreme atrophy of all the papillae. The surface is glazed, shiny, and atrophic, and superimposed on the dorsal aspect are two characteristic verrucous lesions, not warts, but verrucous leukoplakia. On the under surface of the tongue are patches of Grade 2 and Grade 3 leukoplakia.

The tendency of leukoplakia to become verrucous is common, especially in older people. The buccal mucosa near the commissures is a common site, since the expelled smoke acts as an irritant. This man smoked two to three packages of cigarettes daily for many years. Irritation from the heat and the products of combustion will stimulate a verrucous reaction where the papillae are atrophied, as in the bald tongue of syphilis. Verrucous leukoplakia over any length of time is apt to become malignant. It is just a question of time.

This case should be treated as if it were a verrucous malignancy of the tongue, which in syphilitic glossitis is often multiple rather than a single lesion. Any process that grows in a verrucous manner is apt to stay relatively benign for years.

I should recommend electrosurgery, with use of the wire loop with the cutting current. X-rays or radium should never be used in the leukoplakia of syphilitic glossitis, especially if the lesion has become malignant. The percentage of cures in malignancy of the syphilitic tongue is very low.

DR. MAURICE M. TOLMAN: Zero.

DR. FRANCIS P. MCCARTHY: But when you have a warty type, such as a filiform wart, the results may be favorable. I believe this is a true malignant lesion of a verrucous nature which would lend itself to removal by electrosurgery.

DR. MAURICE M. TOLMAN: I go along with everything you said. At one time, as a result of adverse circumstances, we investigated a number of these cases over a long-time follow-up, and we found several factors which contradict one point—that the percentage of carcinomatous degeneration in syphilitic glossitis is extremely high and the percentage of cures extremely low.

DR. FRANCIS P. MCCARTHY: The Palmer Memorial group have been using electrosurgery in cancer of the mouth, and the postoperative reactions are much milder than in cutting surgery.

DR. HARVEY B. ANSELL: Is this lesion malignant or premalignant?

DR. FRANCIS P. MCCARTHY: I should regard it as premalignant, whether the microscope shows it in a single biopsy specimen or not, and would treat the lesion as a malignant verrucous neoplasm.

DR. GEORGE E. MORRIS: I should like to suggest a diagnosis of tertiary syphilis. When I was at Bellevue Hospital years ago, we had cases just like this. We had difficulty getting them under control with potassium iodide or bismuth. This is syphilitic glossitis.

DR. FRANCIS P. MCCARTHY: The evolution of syphilitic glossitis shows a primary endarteritis with a high spirochetal content in the tongue. It is a mobile organ subject to irritation, and, as the endarteritis progresses, the blood supply is markedly reduced, resulting in atrophy of the overlying papillae. The condition is an end result of untreated secondary syphilis. There is no evidence that antisyphilitic treatment is of any value in these cases.

DR. MAURICE M. TOLMAN: It makes it worse.

DR. FRANCIS P. MCCARTHY: I agree.

DR. HOWARD S. YAFFEE: According to Wile, there was no difference in his series whether they excised the lesion or removed it by electrosurgery. Either method was much better than roentgen therapy alone (*J. A. M. A.* 108:374-381, 1937).

DR. FRANCESCO RONCHESE: Any lesion, regardless of size or look, may be considered precancerous. In this case, as long as the histopathology showed no cancer, the treatment of choice should be surface electrocoagulation. I recall a tongue which looked as bad as this one (*Arch. Dermat. & Syph.* 36:347, 1937). Glossectomy was refused. The appearance remained unchanged until the patient died of heart failure, 15 years later.

Cold Urticaria. Presented by DR. G. ROBERT BALER.

A woman, aged 39 years, has noted hives on the exposed portions of the body after exposure to cold. On going out of doors in winter her face,

lips, and eyes have become swollen. Touching anything cold, as leaning against a metal object, results in swelling at the points of contact.

The past history is essentially negative. The patient has been on a weight-reduction diet over the past 10 years and has taken occasional capsules in conjunction with the diet. The last capsule was taken one month ago. Hay fever has been present in mother and son.

Large welts are produced in from one to three minutes on contact with an ice cube. Examination was otherwise within normal limits.

Urinalysis, complete blood cell count, total protein, and electrophoretic pattern of the blood were normal. The serum was negative for cryoglobulins and cold agglutinins.

Discussion

DR. CLEVELAND R. DENTON: This woman should be told that under no circumstances should she immerse herself in cold water, as it might well be fatal. I asked her about the effect of rain on her skin in the summer, and she said it would cause hives. Apparently, it is a matter of temperature differential, as well as the degree of low temperature that causes her urticaria. A similar patient with cold urticaria went into syncope when his four extremities were immersed in cold water in the course of investigation of his cold allergy.

DR. OTIS F. JILLSON: This type of case gives us the opportunity to become internist, and this has been well carried out here. In all these cases of cold urticaria a serologic test for syphilis should be carried out, as cold urticaria may be the presenting symptom of paroxysmal syphilitic cold hemoglobinuria. If the serologic test for syphilis is positive, tests should be carried out for cold hemolysins. Next, it is necessary to test for cryoglobulins, as two-thirds of the reported cases are associated with cryoglobulinemia, aside from those cases associated with kala-azar or subacute bacterial endocarditis. In most of these cases these tests will be negative and the diagnosis will then be that of essential cold urticaria.

DR. MAURAY J. TYE: What has been the experience of the members as to prognosis? Some cases I have seen have cleared.

DR. ROBERT BALER: I recall a report about two years ago of a patient in whom cold urticaria developed after ingestion of something containing acetic acid, such as sauerkraut and vinegar. Without that, there was no urticaria. The mechanism of cold urticaria is rather vague, but the predominating opinion is that it is an antigen-antibody reaction. You can produce passive transference, but I have not tried it. Repeated exposure to cold can exhaust the reaction. Rothman feels it may be just an exaggeration of a normal physiological response and that it may be a hypersensitivity mechanism.

DR. ALFRED HOLLANDER: It is my understanding that heat and cold urticaria are not antigen-antibody reactions.

DR. CHARLES W. O'NEILL: This patient has been on reducing pills for a long time.

DR. OTIS F. JILLSON: As for passive transfer tests, in cold urticaria it is necessary to challenge the site of injection within five to six hours following injection of the serum. You can not wait a day or two for the irritative reaction of the serum to subside before carrying out the final phase of testing. Since these cases are rare, it might be of interest to carry out passive transfer tests here.

Lepromatous Leprosy with Acute Lepra Reaction. Presented by DR. JOHN S. STRAUSS.

Porphyria Cutanea Tarda. Presented by DR. EDMUND F. FINNERTY JR.

Hereditary Hypercholesteremic Xanthomatosis. Presented by DR. DAVID FOLAN.

A Case for Diagnosis (Dermatitis Herpetiformis?). Presented by DR. MAURAY J. TYE.

Lichen Planus. Presented by DR. MAURICE TOLMAN.

Keratoderma Climactericum. Presented by DR. E. GLICKLICH.

Systemic Lupus Erythematosus. Presented by DR. MAURAY J. TYE.

Lupus Erythematosus (Classification?). Presented by DR. MAURAY J. TYE.

Condylomata Acuminata. Presented by DR. PAUL J. CATINELLA.

A Case for Diagnosis (Primary Syphilis in Six-Year-Old Child?). Presented by DR. BERNARD APPEL.

Keratoderma (Psoriasis? Pityriasis Rubra Pilaris?). Linear Nevus of the Neck with Superimposed Verruca Vulgaris. Presented from BOSTON CITY HOSPITAL.

Alopecia Prematura.

A Case for Diagnosis (Lichen Sclerosus et Atrophicus? Balanitis Xerotica Obliterans?). Presented by DR. BERNARD APPEL.

A Case for Diagnosis (Porokeratosis of Mibelli?). Presented by DR. WILLIAM R. HILL.

A Case for Diagnosis (Herpes Simplex? Chancroid? Primary Syphilis?). Presented from BOSTON CITY HOSPITAL.

Late Chronic Radiodermatitis. Presented by DR. JULIUS PICARD.

Keratosis Follicularis. Vitamin A Deficiency. Secondary Alopecia. Presented by DR. HOWARD S. YAFFEE.

A Case for Diagnosis (Epidermolysis Bullosa Simplex, Acquired Type? Brunsting-Perry Syndrome? [Vesicular Eruption Associated with Colitis and/or Pyoderma Gangrenosum]). Presented by DR. SIDNEY ALLMAN, DR. MILTON HELLMAN, and DR. HOWARD YAFFEE.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILOLOGY

Lester Barker, M.D., Chairman
Nathan Sobel, M.D., Secretary

Oct. 7, 1958

Diagnosis: Chronic Bullous-Ulcerative Disease. Presented by Dr. Frank E. Cormia.

Discussion

Dr. Abraham J. Orfuss: In looking over the protocol I saw no indication that the γ-globulin determination was done.

Chairman Barker: The cryoglobulins were negative.

Dr. Orfuss: The γ-globulins.

Dr. Frank E. Cormia: She had a starch gel electrophoresis pattern, and the γ-globulins are normal.

Dr. David Bloom: In spite of a normal γ-globulin in the serum, I should suggest the diagnosis of pyoderma gangrenosum, which is very frequently associated with arthritis and not necessarily with ulcerative colitis. I believe that the patient will benefit by a strongly supportive therapy. Even γ-globulin injections may be of benefit in spite of a normal content in the serum.

Dr. Beatrice Kesten: I agree with Dr. Bloom that this belongs in the group of allergic vasculitis, namely, dermatitis nodularis necrotica. The psychogenic aspects are probably secondary. She has sinusitis and at one time had lesions on her hands. The one therapy that seemed to have been somewhat helpful, from her story, was bed rest and cortisone. I should suggest this therapy combined with erythromycin.

Chairman Barker: I should suggest a diagnosis of livedo reticularis with ulcerations. The ulcerations usually occur during cold weather, although Kierling reported on a series where the ulcerations developed only during hot weather. Dr. Nelson presented a case of livedo reticularis and ulcerations with hypogammaglobulinemia.

Dr. Carl T. Nelson: This patient has electrophoretically normal serum globulins and no cryoglobulins. Therefore, it is very hard for me to make a diagnosis of hypogammaglobulinemia or antibody deficiency syndrome in this instance. I should be more inclined to agree with Dr. Kesten's suggestion that this may be a case of so-called allergic vasculitis with ulcerations. In the few cases of allergic vasculitis we have had, the patients seem to have done extraordinarily well on corticosteroids.

Submitted for publication Jan. 28, 1959.

Diagnosis: Adenoma Sebaceum (Treatment by Dermabrasion). Presented by Dr. Douglas P. Torre for Dr. Mark Marciano.

Discussion

Dr. David Bloom: The treatment is successful, but the hyperpigmentation, which was caused by the dermabrasion and persisted for more than six months, is an observation which should deter the dermatologist from using this mode of therapy in darkly pigmented patients.

Dr. Juan Larralde: I can mention two cases of the type of adenomas in which the patient was hyperpigmented and later on developed depigmentation. One patient improved, but the other was not improved by dermabrasion. One has to see how long that improvement is going to last. They usually recur.

Dr. Sidney J. Robbins: In the early phases of dermabrasion, we treated a mentally defective female with adenoma sebaceum at "Skin and Cancer" over a period of about a year. This girl of 16 was of Puerto Rican descent, with a hyperpigmented skin. We tried out various areas individually because we were afraid of the possible resulting hyperpigmentation or depigmentation after planing. We found eventually that the lesions disappeared very beautifully. There was temporary hyperpigmentation and then, after about six months, the skin was completely clear without pigmentary changes.

I also have treated a case of a 23-year-old woman for the same condition; a white girl who had adenoma sebaceum and she was treated with dermabrasion in fractionated doses on small areas. The results in this case have been permanently satisfactory with a very beautiful cosmetic effect.

Dr. Maurice J. Costello: Dr. DeFeo and I had the good fortune of obtaining an excellent result in treating a child of Anglo-Saxon background who had adenoma sebaceum lesions on the oval of the face. However, the lesions on the nose we did not treat with dermabrasion but with electrocautery. This was about a year and one-half ago. We think it was the best result we have ever obtained with dermabrasion in any type of skin condition. It is indicated perhaps in selected cases. It should not be performed on the Negro.

Dr. Daniel P. Torre: We found that by not using freezing with dermabrasion we seem to get much less pigmentation. I believe adenoma seba-

ceum lesions can be removed with microabrasion without refrigeration or infiltration anesthesia. A small dental type burr fitted to a wire brush machine easily removes individual lesions. The gross type abrasion for this type of lesion is probably not necessary.

Diagnosis: Lichen Planus Hypertrophicus. Reason for Presentation: Therapeutic suggestion. Presented by DR. ADRIAN NEUMANN.

Discussion

DR. VICTOR H. WITTEN: Providing this is lichen planus, I think it would be worth while injecting the base of the lesion with hydrocortisone acetate suspension (Merck, Sharp & Dohme) which is available 25 mg. per milliliter. One milliliter should be adequate for the lesion. We have used some of the specially prepared Upjohn material (200 milligrams of hydrocortisone acetate per milliliter) for this purpose. It is well tolerated in areas such as this. The local atrophy of the tissues which follows thus far has been no greater than with the weaker concentrations (as with the 25 mg. per milliliter suspension). I should guess that one such injection should prove effective for weeks, maybe months, perhaps as long as the crystals persist in the tissues.

Diagnosis: Adenoma Sebaceum (Treatment by Dermabrasion). Presented by DR. DOUGLAS P. TORRE for DR. MARK MARCIANO.

Anaphylactoid Reaction to Pituitrin Injection. Presented by DR. MILTON REISCH for DR. MARK MARCIANO.

Diagnosis: Lichen Planus-like Eruption Caused by Color Developer. Presented by DR. ORLANDO CANIZARES.

Case for Diagnosis: Dermatitis Medicamentosa? Lupus Erythematosus, Disseminated, Discoid? Premycotic Mycosis Fungoides? Presented by DR. HERBERT SPOOR.

Diagnosis: Boeck's Sarcoid Responding to Aralen. Presented by DR. MILTON REISCH for DR. MARK MARCIANO.

Diagnosis: Verrucous Lesions at Site of Tuberculin Test. Presented by DR. ORLANDO CANIZARES and DR. EDWARD SHAPIRO (by invitation).

Diagnosis: Hypertrophic Lichen Planus; Licheno Planopilaris. Presented by DR. ALEXANDER W. YOUNG for DR. MARK MARCIANO.

Psoriasis. Presented by DR. ORLANDO CANIZARES.

Linear Scleroderma. Presented by DR. FRANK E. CORMIA for DR. MARK MARCIANO.

Parapsoriasis? Presented by DR. JOHN DOUGHERTY for DR. LEO LESE.

Vitiligo with Multiple Sutton's Nevi. Presented by DR. HARRY KATZ for DR. ROBERT ABEL.

Morphea of Scalp—Partial Return of Hair Following Hydrocortisone Injections. Presented by DR. CHARLES SHEARD.

Psoriasis (Coincident with Chemical Remission of Nephrotic Syndrome). Presented by DR. HERBERT SPOOR.

Sarcoidosis. Presented by DR. DOUGLAS P. TORRE for DR. LEO LESE.

Urticaria Pigmentosa. Presented by DR. ALEX. W. YOUNG JR. for DR. ROBERT ABEL.

NEW YORK DERMATOLOGICAL SOCIETY

J. Lowry Miller, M.D., President
Frank E. Cormia, M.D., Secretary

Oct. 28, 1958

Recurrent Herpes Simplex with Erythema Multiforme and Stomatitis. Presented by DR. EUGENE F. TRAUB.

A man, aged 27 years, has had a recurrent eruption since the age of 8 years. His first attack occurred in July, 1939, after he had been out in the sun, and they have recurred ever since, although not every year. He has been free for as long as two years but had two attacks this summer. As a schoolboy, before he learned that the sun could cause the outbreaks, his lower lip would be involved almost from one corner to the other. He has had only a single blister on the upper lip. He has seldom been without at least one lesion in summer, he has an occasional one in the fall but few, if any, in the winter.

The attacks always develop in the same way. The lower lip feels hot and a slight swelling is followed by a pinhead-sized spot which becomes a blister in two or three days. By that time the lip is swollen to at least one-third larger than normal and both lips are inflamed. Two or three blisters may form. By the end of a week, these break and form a yellow erosion, and a crust builds up which turns dark brown by the 10th day, approximately. A few days later there may be a bloody oozing, often without apparent cause, and the lesion is coal black by the third week, when the eruption shows signs of clearing.

Ten days to two weeks after the initial lesions appear on the lips, blisters form on the hands and feet on erythematous bases which grow until the largest is about the size of a dime and iris-shaped. His hands become covered; there may be as many as 125 lesions on one hand and arm, and it is impossible even to button his shirt. The feet are usually less severely involved. After a few days the lesions on the extremities develop a central purplish discoloration, which increases slightly in size. At about the same time that the eruption

Submitted for publication March 25, 1959.

appears on the hands, the mouth, tongue, and gums become involved so that it is almost impossible for the patient to eat. The tongue is coated white; his eyes become inflamed, and lesions develop inside the nose, usually with epistaxis. By the beginning of the fourth week the eruption begins to clear, but the marks remain conspicuous for from four to six months.

The eruption present today has about run its course, and the inflamed areas on the lips, hands, and feet merely mark the sites of the lesions described above.

The hematocrit and urine were normal. Biopsy has not been performed.

Treatment has consisted of 10 weekly smallpox vaccinations, x-ray irradiation to lip lesions at the time of onset, and two injections of corticotropin (ACTH). Local treatment has consisted of mouth washes and mild, soothing ointment.

Discussion

DR. CARL T. NELSON: This fits in with the type of erythema multiforme described by N. P. Anderson and others, in which there is a preceding or associated herpes simplex infection. In this case, I gather, the herpes lesions precede the erythema multiforme. The herpes runs its course and then the patient develops lesions of erythema multiforme and stomatitis. For this reason I should conclude that the stomatitis is that of erythema multiforme rather than that of herpes simplex. This is important, because true herpetic stomatitis is a manifestation of primary, rather than recurrent, infection with this virus. Herpes simplex is a systemic infection in many people, and it certainly is in this patient. This is the type of case where herpes virus is widespread in the body and may be isolated from the spinal fluid and elsewhere.

Dr. Traub asked for suggestions for therapy. Treatment with homologous herpes vaccine has been shown to be ineffective, and I hold very little brief for the use of smallpox vaccine in the treatment of herpes. It has not been demonstrated to have any clear-cut influence in preventing recurrent attacks. Attempts to prevent recurrent herpes by vaccination with heterologous virus presumably are based on the phenomenon of viral interference. It was once thought that infection of susceptible cells with one virus would effectively preclude infection with another viral agent. However, this view has now been discarded, since it has been clearly demonstrated that the same cell can be infected simultaneously with more than one type of virus particle. Antihistaminics also have not been found to prevent recurrent herpes, although their use was based on good experimental evidence. You will recall that Good and Campbell were able to precipitate recurrent encephalitis in herpes-infected rabbits by inducing anaphylactic and histamine shock in these animals. This raised some vain hopes that antihistaminics might be useful in preventing recurrent herpes in man.

It is not the herpes simplex of the lip that bothers this patient so much as the erythema multiforme component, which I interpret as an allergic response to the herpetic infection. For this reason I would not be against giving corticosteroids in significant amounts to this patient. I feel that he already has herpes virus so widely distributed in his tissues that the administration of corticosteroids would not spread the infection any further.

DR. GEORGE M. LEWIS: I would support Dr. Andrews in not advising corticotropin (ACTH) or cortisone, chiefly on theoretical grounds. Dr. Nelson's comments are interesting, but I am convinced that some of the cases treated with smallpox vaccine have had a satisfactory result. The reason may not be known, and it may not be any of the theories that have been put forward up to this time. X-ray therapy in fractional dosage is often very valuable. Perhaps more effort should be made to protect against solar exposure by sun-screening or antimalarial preparations.

DR. A. N. DOMONKOS: I have had under observation a woman of approximately 40 years with similar lesions of herpes simplex and erythema multiforme. The herpes lesions are on the sacral area and the erythema multiforme lesions surround that area and are also present on the hand. We have tried γ-globulin, but she invariably returns and begs for smallpox vaccination, which seems to be the only thing that helps. She will stay away for a year and then comes back for more.

DR. FRANK E. CORMIA: I am confused as to the relationship between herpes simplex and the subsequent erythema multiforme. At least two of the members have spoken of a wide systemic invasion of virus, and I assume they refer to herpes virus. As far as I know, nobody has found herpes virus widespread in erythema multiforme. I wonder whether that is not as Dr. Nelson has depicted in the experimental animal, the herpes being an incidental complication precipitated by the allergic or infectious response. If that is the case, and I do not see that we have proved it is not, I can see no contraindication to the use of steroids in erythema multiforme.

DR. M. J. COSTELLO: I have seen a lot of patients with erythema multiforme through the years. I have the special privilege of seeing those at Willard Parker Hospital and can not say I have seen herpes simplex with erythema multiforme often. I think it is not common. The herpes which occurs as part of erythema muliforme may be a herpes simplex that would occur with any other infection, such as pneumonia or typhoid. In regard to therapy, one can not think of a more serious condition than Stevens-Johnson's syndrome

of the malignant type, and steroids have been lifesaving. Patients will die if it is not given. The mortality in the malignant form was nearly 50%, but we have not lost a patient since the steroids became available. Corticotropin (ACTH) is administered intravenously and then by mouth if the patient can swallow. In the treatment of the severe Hebra type, where there is high fever without ocular involvement, the corticosteroids will save the patient weeks of suffering.

DR. A. C. CIPOLLARO: Nelson Paul Anderson wrote an excellent and comprehensive article on the relationship of herpes simplex to erythema multiforme. He advocated smallpox vaccines for the treatment of such cases and reported good results. The diseases in combination are not common, but we undoubtedly overlook a good many of them.

DR. DOUGLAS TORRE: How is smallpox vaccine given these days—intradermally, or by the old scratch method? In regard to the use of γ-globulin, we have had two cases at New York Hospital, one with recurrent hérpes simplex and one with aphthous stomatitis, which seemed to respond to administration of γ-globulin at two-week intervals.

DR. EUGENE F. TRAUB: I do not believe the diagnosis of these cases could be missed. This patient goes through a course of events that would require no special inquiry, and this is the first such patient I have seen in 40 years with this exact course. The matter of sun protection is difficult, because if this patient is out for even half an hour, without unusually bright sunlight, he may have an attack. The question of mouth hygiene should be looked into. His attacks have come so close together that we were not able to do much. He was able to predict what was going to come, but in neither attack did x-rays abort it. He has been vaccinated by the scratch method on about 10 occasions, and something seemed to abort the second attack slightly. He was also given two injections of corticotropin, very gingerly, because he was going away on his honeymoon. Some of these cases have been reported to do well with γ-globulin. It has certainly been my impression that 50% or more of patients seem to improve or have remissions of attacks after smallpox vaccination. If you can accomplish anything in these severe cases, it is worth while. As Dr. Nelson mentioned, direct inoculations from the vesicles have been tried in these cases but have not proved successful. I have found that autogenous vaccine did not necessarily do as well as one from stock.

Erythroplasia of Queyrat—Squamous-Cell Epithelioma. Presented by DR. GERALD F. MACHACEK.

A white man, aged 54 years, has noticed on his penis for the past five months a red patch which itches. About one month ago an elevated area appeared in the center of the patch. He has been cleaning his prepuce and glans daily with soap and water. The patient states that as a young man he had a chancre but had no treatment.

There is a sharply demarcated erythematous plaque on the glans penis which presents an elevated, warty area about 1 cm. in diameter. In the right inguinal region two small, firm glands can be palpated.

Serologic tests for syphilis are negative.

Discussion

DR. M. J. COSTELLO: I can not agree entirely. It is an unusual case. The prepuce and portion of the glans not covered by the prepuce are not involved. It may be some form of psoriasis.

DR. EUGENE F. TRAUB: Clinically, the lesion at the tip of the penis certainly looked suspicious. Some thickening was visible, and maybe it could have been felt as a hard lesion. The nodes may be purely inflammatory, although they could be very important.

DR. CARL T. NELSON: The lesion on the glans, stony-hard on palpation, together with the enlarged lymph nodes, would make me agree with the diagnosis.

DR. WILBERT SACHS: I have never found a single case in the literature that proves that erythroplasia has degenerated into a malignant process. In order to prove the diagnosis one would have to take biopsy specimens—one from an area that is not ulcerated or hard and another from the edge of the lesion.

DR. GEORGE C. ANDREWS: I agree with the diagnosis of erythroplasia with malignant degeneration.

DR. A. N. DOMONKOS: I am sure it is carcinoma of the penis; whether we are going to call it erythroplasia or not is a matter of definition. The velvety, shiny appearance is characteristic of erythroplasia of Queyrat. The urological department at Presbyterian Hospital has had a series of unfortunate occurrences; cases treated locally with arsenic have metastasized, with death, so the present policy is to perform complete amputation of the penis.

DR. M. J. COSTELLO: Dr. Sachs, what do you think this is?

DR. WILBERT SACHS: I think there is ulceration and lymph nodes in the groin. He certainly has infection, and the lymph nodes may be infectious or they may be malignant. The ulceration should be biopsied to rule out the possibility of malignancy.

DR. M. J. COSTELLO: The lesion looks like an epithelioma. However, that portion of the glans which is covered, where the prepuce is normally over the corona, is not involved. How could it be so specific? That would be an unusual configuration for a carcinoma.

DR. WILBERT SACHS: It would be a little unusual to have a carcinoma develop so quickly.

DR. GERALD F. MACHACEK: It is a question of definition. Erythroplasia, to my mind, is a neoplasm in situ. Some cases of balanitis should never have been called erythroplasia. There are cases in which arsenic should never be used.

DR. WILBERT SACHS: Arsenic should never be used in any malignant lesion of the penis—basal- or prickle-cell lesions, Bowen's disease, or anaplasia. In the cases I described and the pathology I described—cases most of you know about and mostly in older men—the diagnosis of erythroplasia was undisputed and did not involve malignancy.

Mycosis Fungoides of Thirteen Years' Duration. Presented by DR. J. LOWRY MILLER.

Discoid Lupus Erythematosus with Extensive Hand Lesions. Presented by DR. DOUGLAS TORRE.

Infectious Granuloma. Presented by DR. CARL T. NELSON.

A Case for Diagnosis (Pemphigoid?). Presented by DR. FRANK E. CORMIA.

A Case for Diagnosis (Pustular Psoriasis?). Presented by DR. A. N. DOMONKOS.

Cavernous Angioma. Presented by DR. FRANK E. CORMIA.

Porphyria Cutanea Tarda with Scleroderma and Calcium Deposits. Presented by DR. GEORGE C. ANDREWS.

A Case for Diagnosis (Chronic Vulvar Lesions [Behcet's Syndrome?]). Presented by DR. FRANK E. CORMIA.

A Case for Diagnosis (Hailey-Hailey Disease of the Mouth?). Presented by DR. JOHN W. DOUGHERTY.

Hemolymphangioma Circumscriptum. Presented by DR. M. J. COSTELLO.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

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Oct. 17, 1958

Urticaria Pigmentosa. Presented by CAPT. ROBERT A. NEILL (MC), U. S. Army (by invitation) and CAPT. ALBRECHT F. J. SOMMER (MC), U. S. Army (by invitation).

A 39-year-old woman has had small brownish lesions on the trunk for four years, gradually increasing in number and spreading over the neck, arms, and knees. The lesions wheal and itch upon exposure to cold and heat and when the patient is under emotional stress. She states that her skin flushes during these episodes.

Numerous small, light to dark brown maculopapules arranged along the lines of cleavage are present over the neck, trunk, upper extremities, and knees. They wheal readily upon light stroking.

Urticaria Pigmentosa. Presented by CAPT. ROBERT A. NEILL (MC), U. S. Army (by invitation).

A 3-month-old Filipino girl began to develop skin lesions during the second week of life, and they have continued to form. The mother states that the lesions begin as "reddish bumps" which turn brown and sometimes "welt" for short periods. During the past two weeks the child has had several episodes of intense flushing, lasting for several minutes. These flushes start over the head and progress inferiorly to involve the entire body. In the past week, numerous bullae have appeared.

There is a generalized eruption consisting of brownish macules, papules, and nodules of varying size. Darier's sign is positive.

Submitted for publication Jan. 15, 1959.

Laboratory and x-ray studies are normal, except for slight hypochromic anemia and questionable periosteal reaction in both humeri.

Discussion

DR. EDWARD J. RINGROSE: The generalized flushing which spreads over the body is apparently due to the liberation of histamine. There is a good article on this subject in the *Acta pediatrica.* A child described in this article went into shock several times, apparently due to the liberation of histamine from several nodular lesions. After several of the larger nodules were removed, the spontaneous histamine shock no longer occurred.

DR. MORTIMER S. FALK: A prolonged course of sublingual deoxycorticosterone acetate tablets might be of benefit. Urbach, Jacobsen, and Bell (*J. A. M. A. Arch. Dermat. & Syph.* 70:675-676 [Nov.] 1954) presented a patient with urticaria pigmentosa who was significantly improved after taking DOCA for six months. It would be interesting to evaluate further this form of treatment.

DR. ROBERT A. NEILL: In infants, the onset at birth is seen in only about 10% of the cases and bulla formation is found in about 5% of cases reported in the literature. Total-body x-ray films of the infant showed some questionable thickening of the humeri.

In both cases the flushing phenomenon is very interesting. It is not too definite in the adult and is probably not a true flush, but in the baby it is very characteristic of the flush described in the functioning carcinoid by Dr. Kierland in the

A. M. A. ARCHIVES OF DERMATOLOGY of January, 1958. This is a transient flush, lasting 10 minutes or less, starting on the face and progressing inferiorly. Sometimes there are patches of cyanosis. A hydroxyindoleacetic acid determination was negative on the baby, but the adult gave a positive reaction.

It has been known for some time that mast cells secrete histamine and heparin, but there is some question as to whether they secrete hyaluronic acid, hyalurodinase, or serotonin. Rats and mice definitely have serotonin in their mast cells, but this has not been found in man, dog, or the cow. Probably the best idea now is that serotonin liberates histamine and histamine is responsible for the flushing.

Trichophyton Tonsurans Infection of the Scalp.

Presented by DR. HERBERT L. JOSEPH and DR. THOMAS J. SULLIVAN (by invitation).

The patient is a 23-year-old Mexican housewife, who came to the United States two months ago. Shortly after her arrival, she noted itching, pain, and loss of hair at the vertex of the scalp. She recalls having used the comb of a woman with a similar condition in Mexico about one week before her departure.

There are grouped 0.5 to 1.5 cm. papulopustules at the vertex of the scalp. The inflammatory reaction has subsided under treatment, there having been a large granulomatous area at first. One month ago her 8-year-old son was also found to have tinea capitis due to Trichophyton tonsurans.

The culture is positive for T. tonsurans. Treatment has consisted of hot compresses, Triacetin spray, and potassium iodide by mouth.

Tinea Capitis Due to Trichophyton Tonsurans.

Presented by DR. PAUL M. CROSSLAND and DR. WALTER E. WEBER.

Four Mexican siblings, three boys, aged 8, 7, and 5 years, and one girl, aged 2, moved to Santa Rosa, Calif., about three years ago. They were found to have scaling patches with broken-off hairs in August, 1958. This was said to have been present for about two years in the boys and four months in the girl. The 7-year-old boy developed kerion in June, 1958. The others have shown a few pustules and scaly patches in the scalp.

X-ray epilation was performed on the three boys 23 days ago with the Adamson-Kienbock technique, employing the following factors: 350 r in air to each of five focal points, TSD 25 cm., 90 kv., 5 ma., HVL 0.84 mm. of aluminum. The girl received x-ray 17 days ago with the same technique and factors, with use of 340 r to each of the five focal points.

Within one week after x-ray the kerion was improved. Tenderness, edema, and folliculitis were substantially reduced. Defluvium on all three boys' scalps began on the 16th day and is now complete, on the 23d day. The girl's hair is now beginning to fall.

Discussion

DR. THOMAS J. SULLIVAN (by invitation): When first seen in our clinic, the adult woman had lesions which fit the classical description of Majocchi's granuloma or granuloma trichophyton.

DR. HERBERT L. JOSEPH: I did not see the adult patient at first. At present, she has what appears to be a kerion. In adults there is usually little inflammatory reaction. Kerion and the other inflammatory reactions are more frequent in children with T. tonsurans tinea capitis.

The different clinical types of reactions in the scalp are well illustrated in the four children—indolent, with little or no reaction, seborrhea-like, and mildly inflammatory with pustules and kerion.

DR. PAUL M. CROSSLAND: Since these children were the first cases of T. tonsurans infection in our community, we thought we should epilate for two reasons. First, this is undoubtedly the most effective form of treatment, and safe if properly conducted. Second, this might forestall an epidemic of T. tonsurans infections.

Tinea capitis and other manifestations of infection with T. tonsurans are becoming more common in northern California. We should dispel the notion that tinea capitis occurs only in children. T. tonsurans is being brought to this country from Mexico. In some parts of Mexico it is the causative organism in 92% of fungous infections. Recently Rantz et al. (Rantz, L. A.; Halde, C; Newstrant, A. B., and Kettner, B. S.: Fungus Diseases in Northern California, *California Med.*, 89:245-249 [Oct.] 1958) found 90 positive cultures of T. tonsurans among 542 cases of superficial fungus disease studied by them at Stanford University Hospital Clinic.

In the scalp infections caused by T. tonsurans, the clinical manifestations may vary greatly. There may be only a few hair stubs and slight scaling simulating seborrhea sicca. On the other hand, some cases show alopecia, scarring, follicular plugging, and even telangiectasia, presenting the clinical appearance of chronic discoid lupus erythematosus of the scalp. In cases showing inflammatory reaction, there may be mild perifolliculitis, furuncles, frank kerion, or a granulomatous reaction simulating perifolliculitis capitis abscedens et suffodiens. According to Pipkin (Tinea Capitis in Adult and Adolescent, *A. M. A. Arch. Dermat. & Syph.* 66:9-40 [July] 1952) the incidence of kerion is 5% in adults (18% in children) with T. tonsurans scalp infections. Granuloma trichophyticum occurs in 5% of adult patients, L. E.-like lesions in 5%, and glabrous skin lesions in 59%. The

only constant findings in all cases are hair loss, scaling, and infected stubs. Infected hairs show no fluorescence under Wood's light. However, blonde, gray, or white infected hairs appear a dull grayish-white which is different from their normal color.

In view of the wide range of clinical manifestations, we should raise our index of suspicion in regard to T. tonsurans infections. The disease should be included in the differential diagnosis of discoid lupus erythematosus of the scalp, seborrheic dermatitis and any inflammatory reaction on the scalp. Patients with T. tonsurans infections of the glabrous skin or nails should be given a close examination of the scalp for any sign of scaling or hair stubs, because of the frequent association of scalp lesions with glabrous skin (59%) or nail (25%) lesions.

The treatment of choice for tinea capitis due to T. tonsurans is temporary epilation of all scalp hair by means of x-rays. I believe this should be done even in the presence of inflammatory reaction or granuloma formation, because it may take 6 to 12 months for such cases to clear. In the meantime, many other persons may be infected. In one of the cases we have presented here, the inflammatory reaction was greatly reduced within a week after the x-ray epilation was administered.

Using the Kienbock-Adamson method of x-ray epilation, the dose administered to each of the five focal points on the scalp should be 350 r for children and 400 r for adults. The half-value layer of the radiation used should not exceed 1 mm. Al. After defluvium has occurred, very careful and protracted manual depilation should be done to be sure that every infected stub is removed. Recurrences are frequent if this is not done.

Cipollaro and Ruppe (Cipollaro, A. C.; Kallos, A., and Ruppe, J. P.: Measurements of Gonadal Radiations in the Treatment of Tinea Capitis, Unpublished) have measured to gonadal dose during x-ray epilation and found it to be about 20 millirems for an entire epilation. This dose can be reduced to practically zero if a sheet of lead rubber 4 mm. in thickness is placed under the patient and another over him, extending from the umbilicus to the knees.

Spreading the disease in a community can be avoided if the first cases discovered are treated by x-ray epilation. All the other members of the patient's family should be thoroughly examined for evidence of the fungus. All cases should be isolated until cured.

Public health authorities in this country should follow the example of Israel (Dostrovsky, A.; Kallner, G.; Raubitscheck, F., and Sagher, F.: Tinea Capitis: An Epidemiologic, Therapeutic and Laboratory Investigation of 6,390 Cases, *J. Invest. Dermat.* 24:195, 1955), where each immigrant is examined carefully for fungus infection of scalp, skin, or nails before entry is permitted. Infected persons are placed in quarantine and treated until cured before entering the country. This has been a successful way of preventing the spread of endothrix Trichophyton infections which are prevalent in the surrounding countries. Israeli Health authorities use the Kienbock-Adamson technique of x-ray epilation to cure the endothrix scalp infections, which are principally caused by T. violaceum and T. schonleini. They have performed thousands of such x-ray epilations successfully and without harm to the patients.

We should not hesitate to recommend this procedure when it is indicated. It is our duty to perform epilations if we are properly trained and have the proper equipment.

DR. KEMP H. DOWDY: Those of us who trained in the East learned to epilate with x-ray without hesitation. Unfortunately, there is great fear of this in California, and, as a result, patients are being deprived of an excellent form of treatment. I agree with Dr. Crossland that it is a safe procedure when properly done, and I have never encountered any difficulties whatsoever.

DR. NORMAN E. LEVAN: We are seeing an increasingly high percentage of T. tonsurans infections in the Central Valley of California.

I must be counted among the cowards regarding x-ray epilation. I presented a case before the Los Angeles Dermatology Society with both alopecia areata and tinea capitis due to T. tonsurans. This occurred in a very "suit-conscious" family.

Addendum

These cases were treated before the advent of the new drug, Griseofulvin, which has proved of such great value in the treatment of tinea capitis that it may obviate the need for x-ray epilation.

Generalized Pustular Psoriasis. Presented by DR. CONSTANCE M. BUNCKE and DR. FRANCIS J. SULLIVAN (by invitation.)

A Case for Diagnosis: Hailey-Hailey Disease? Presented by DR. WALLACE M. PROCTOR.

Case for Diagnosis: Primary Systemic Amyloidosis? Presented by DR. JOHN H. EPSTEIN and DR. WILLIAM W. SERVICE (by invitation).

Case for Diagnosis: Scleroderma with Lichen Sclerosus et Atrophicus. Presented by DR. RALPH T. BEHLING.

Porokeratosis. Presented by DR. MARTIN ASCH.

Syringoma. Presented by CAPT. GEORGE B. SKIPWORTH (MC), U. S. Army, (by invitation).

Generalized Progressive Scleroderma. Presented by DR. EARL R. CLAIBORNE.

Case for Diagnosis: Lymphoblastoma? Granuloma? Presented by DR. BARTHOLOMEW J. SPENCE JR.

Case for Diagnosis: Presented by DR. GEORGE T. WILSON.

The New, Newer, and Newest

Advance information indicates that the Symposium on Griseofulvin and Dermatomycoses, to be held in Miami, Fla., Oct. 26-27, might well turn out to be a historic occasion. Harvey Blank, because of a grant to the University of Miami School of Medicine from the McNeil Laboratories Division of Johnson & Johnson, was able to arrange for a meeting that is international in scope and all-embracing. Because of the significance of the development of Griseofulvin, *New, Newer, and Newest* herein publishes the tentative program, and the ARCHIVES has arranged to publish all of the papers as soon as possible after the meeting. The meeting is to be in the Dupont Plaza Hotel in Miami. It is open to all physicians and investigators.

Foreign Participants

Campbell, A. H.: Glaxo Labs., England
Childs, K. J.: Glaxo Labs., England
Desai, S. C.: G. S. Medical College, Bombay, India
Gentles, J. C.: Anderson College, Glasgow, Scotland
Gonzalez-Ochoa, A.: Inst. Salub. Enferm. Trop., México, D. F.
Kaminsky, A.: Univ. Med. School, Buenos Aires, Argentina
Latapi, F.: Univ. Med. School, México, D. F.
Paget, G. E.: Imperial Chem. Indust., England
Pardo-Castello, V.: Univ. Med. School, Havana, Cuba
Williams, D. I.: King's College Hosp., London, England
Wrong, N.: Univ. Med. School, Toronto

U. S. A. Participants

Ajello, L.: Communicable Disease Center, Chamblee, Ga.
Blank, H.: Univ. of Miami, Miami, Fla.
Burgoon, C. F.: Skin & Cancer Hosp., Philadelphia
Callaway, J. L.: Duke Univ., Durham, N. C.
Conant, N. F.: Duke Univ., Durham, N. C.
Derbes, V.: Tulane Univ., New Orleans
Dillaha, C.: Univ. of Arkansas, Little Rock, Ark.
Emmons, C.: Nat. Inst. Health, Bethesda, Md.
Ferguson, J.: U. S. Army, Fort Sam Houston, Texas
Gaughran, E. R. L.: Johnson & Johnson, New Brunswick, N. J.
Goldfarb, N.: New York Univ., New York
Grutter, F. H.: Johnson & Johnson, New Brunswick, N. J.
Harrell, E. R.: Univ. of Michigan, Ann Arbor, Mich.
Hildick-Smith, G.: Johnson & Johnson, New Brunswick, N. J.
Kaplan, W.: Communicable Disease Center, Chamblee, Ga.
Kirk, J. M.: Dept. Public Health, Washington, D. C.
Kligman, A. M.: Univ. of Pennsylvania, Philadelphia
Knox, J. M.: Baylor Univ., Houston, Texas
Lazar, P.: Northwestern Univ., Chicago
Lewis, G.: Cornell Univ., New York
Livingood, C. S.: Henry Ford Hosp., Detroit
MacLeod, J.: Cornell Univ., New York
McNall, E.: Univ. of California, Los Angeles
McCuistion, C. H.: Austin, Texas
Mullins, J. F.: Univ. of Texas, Galveston, Texas
Newcomer, V. D.: Univ. of California, Los Angeles
Pillsbury, D. M.: Univ. of Pennsylvania, Philadelphia
Pipkin, J. L.: Baylor Univ., San Antonio, Texas
Prazak, G.: U. S. Army, Fort Sam Houston, Texas
Rattner, H.: Northwestern Univ., Chicago

Robinson, H., Jr.: Univ. of Maryland, Baltimore
Robinson, R. C. V.: Univ. of Maryland, Baltimore
Rosenthal, S.: New York Univ., New York
Roth, F. J., Jr.: Univ. of Miami, Miami, Fla.
Rothman, S.: Univ. of Chicago, Chicago
Sallman, B.: Univ. of Miami, Miami, Fla.
Sams, W.: Univ. of Miami, Miami, Fla.
Schwarz, J.: Univ. of Cincinnati, Cincinnati
Smith, J. G., Jr.: Univ. of Miami, Miami, Fla.
Sternberg, T.: University of California, Los Angeles
Sorenson, L.: Univ. of California, Los Angeles
Sulzberger, M.: New York Univ., New York
Wilson, J. W.: Univ. of S. California, Los Angeles

The sessions will be devoted to in vitro and laboratory studies; animal, pharmacologic, and experimental studies, and clinical aspects to be reported in formal papers and in a round-table discussion.

H. R.

Abstracts from Current Literature

ACQUIRED AGAMMAGLOBULINEMA WITH MULTIPLE ALLERGIES AND PERNICIOUS ANEMIA. R. V. CROWDER JR., W. T. THOMPSON JR., and H. G. KUPFER, A. M. A. Arch. Int. Med. 103: 445 (March) 1959.

A man with acquired agammaglobulinemia starting at 28 years of age also had pernicious anemia and multiple allergies. The immediate type skin reaction to allergens and the delayed type of tuberculin occurred in this asthmatic patient. It is possible that the reagins may be located in the α- or β-fractions or even in more than one fraction in multiple sensitivities. A positive transfer test reaction to dust illustrated the presence of circulating antibodies. Of additional interest, in the presence of infection in this patient, the sedimentation rate was always very low.

LAZAR, Chicago.

TUBEROUS SCLEROSIS IN ADULTS WITH NORMAL INTELLIGENCE. A. KOFMAN and H. H. HYLAND, A. M. A. Arch. Neurol. & Psychiat. 81:43 (Jan.) 1959.

This presents a case of tuberous sclerosis with symptoms developing in a man, aged 62, and without a family history of the disorder. Intelligence was not impaired in spite of cerebral involvement as indicated by focal epilepsy and radiographic findings. The condition may be commoner in adults than is supposed, and adenoma sebaceum need not be associated with other features of tuberous sclerosis.

LAZAR, Chicago.

DIFFERENTIATION OF NEOPLASTIC LESIONS CHARACTERIZED BY LARGE VACUOLATED INTRAEPIDERMAL (PAGETOID) CELLS. E. W. FISHER and F. BEYER JR., A. M. A. Arch. Path. 67:140 (Feb.) 1959.

Histochemical procedures are described which are helpful in the differential diagnosis of the large pleomorphic intraepidermal epithelial cells with optically clear cytoplasm observed in Bowen's and extramammary Paget's disease, malignant melanoma, and intraepithelial carcinoma arising in the cloneogenic zone of the anorectal junction. The results are obtained with a few, relatively simple, histochemical techniques.

LAZAR, Chicago.

IMMUNOCHEMICAL DEMONSTRATION OF FIBRIN IN THE GENERALIZED SCHWARTZMAN REACTION. D. G. MCKAY, D. GITTIN, and J. M. CRAIG, A. M. A. Arch. Path. 67:270 (March) 1959.

Using the fluorescent-antibody method of Coons and Kaplan, the authors were able to demonstrate that the hyaline thrombi in the Schwartzman reaction are primarily composed of fibrin. The thrombosis may be prevented by the use of heparin, warfarin sodium, and streptokinase.

LAZAR, Chicago.

ALDRICH'S SYNDROME (THROMBOCYTOPENIA, ECZEMA, AND INFECTION IN INFANTS). W. KRIVIT and R. A. GOOD, A. M. A. J. Dis. Child. 97:137 (Feb.) 1959.

Seven cases of Aldrich's syndrome were reviewed and studied extensively. All the patients were boys; the syndrome appears to be transmitted as a sex-linked recessive trait. Typically, the onset of melena in the neonatal period was noted in five of the affected children. Despite extensive investigations of the peripheral blood, skin, and lymph node biopsies; globulin and properidin levels, and adrenal steroid physiology, no unusual findings were noted. All attempts at treatment were unsuccessful, though adrenal steroid and systemic estrogen and progesterone therapy ameliorated the eczematoid process.

LAZAR, Chicago.

NECROBIOSIS LIPOIDICA DIABETICORIUM. J. W. KELLEY, Plast. & Reconstruct. Surg. 22:342-347 (Oct.) 1958.

Split-thickness grafts may be the treatment of choice when chronic ulcerations complicate necrobiosis lipoidica diabeticorum. A good result in a 19-year-old woman is described after

local and systemic medical therapy had failed. A three-year observation period followed the surgery, and a review of previous experiences is presented.

LAZAR, Chicago.

RAPID DIAGNOSIS OF HERPES SIMPLEX VIRUS INFECTIONS WITH FLUORESCENT ANTIBODY. JOSEPH Z. BIEGELEISEN JR., L. VERNON SCOTT, and VESTER LEWIS, JR., Science 129:640-641 (March 6) 1959.

The authors prepared fluorescein-tagged specific anti-herpes-simplex antibody which, when reacted with smears prepared from herpes simplex lesions, gave specific positive results. This may become a useful and simple laboratory procedure for the diagnosis of herpes simplex infections.

BLANK, Miami, Fla.

MUCOUS MYELINIC NEUROMAS WITH CENTRO-FACIAL AND LARYNGEAL LOCALIZATION: NEW ENITY? A. BAZEX and A. DUPRÉ, Ann. dermat. et syph. 85:613-641 (Nov.-Dec.) 1958.

A disorder characterized by the appearance in early infancy of confluent nodules on the lips, the tongue, the larynx, the nostrils, and the eyelids. These little tumors correspond histologically to fasciculated myelinic neuromas. The authors were able to find a practically identical observation published by Froboese, in 1923. They believe that this is probably a new entity caused by complex dysraphic difficulties. Numerous excellent pictures and an extensive bibliography are included.

DERBES, New Orleans.

UTILIZATION OF PATHOGENIC TREPONEMA PALLIDUM AS AN ANTIGEN FOR THE COMPLEMENT FIXATION REACTION. A. VAISMAN, A. HAMELIN, and R. PRUDHOMME, Ann. dermat. et syph. 85:642-649 (Nov.-Dec.) 1958.

The source of Treponema is furnished by rabbit testicles infected with the Nichols strain. Spirochetes are placed in suspension in phenolized isotonic saline, after several washings in order to eliminate as far as possible testicular elements. The disintegration is obtained by submitting the suspension to ultrasonic vibrations for 30 minutes. The antigen thus prepared is a very homogeneous opalescent suspension consisting of fine granulations. A total of 2,216 specimens were studied by the T. P. I. technique, of which 1,666 were positive. Of this number, 1,576, or 94.6%, were positive using the T. pallidum antigen; 1,474, or 88.4%, were positive with use of the Reiter antigen, 1,030, or 61.8%, were positive with use of the classic serologic techniques. The specificity of the ultrasonic T. pallidum antigen is thus clearly superior to that of the Reiter antigen and permits the elimination of more false-positive reactions obtained by classic serological techniques.

DERBES, New Orleans.

THE EFFECTS OF INJECTIONS OF SERUM FROM PATIENTS WITH ALLERGIC DERMATOSES INTO THE DERMIS OF GUINEA PIGS. P. TÉMIME, D. PICARD, and A. T. TÉMIME-MORHANGE, Ann. dermat. et syph. 86:5-16 (Jan.-Feb.) 1959.

Authors injected serum from patients suffering from diverse conditions, such as allergic nodular dermatosis, subacute and chronic L. E., urticaria, eczema, etc. into guinea pigs. They found an ecchymosis secondary to a profound dermal arteriolitis of necrotic type seen especially after use of sera from patients with L. E. (two cases), urticaria (four cases), nodular dermal allergide (one case), and erosive ectodermosis (one case). Serum of patients with other dermatoses did not show such phenomena. They suppose that a special substance accounts for these changes, called arteriolotoxin.

DERBES, New Orleans.

VARIATIONS OF SERUM SODIUM AND POTASSIUM IN CERTAIN DERMATOSES AND THE INFLUENCE OF ADMINISTRATION OF STEROIDS. S. M. MILCOU, L. IANCOU, V. SAHLEANOU, and L. MITRACHE, Ann. dermat. et syph. 86:31-40 (Jan.-Feb.) 1959.

In eczema, as well as psoriasis, there exists a parallel increase of serum sodium and potassium which tends to normal after steroid administration. These findings are similar to those which other authors have found in the skin itself in these conditions.

DERBES, New Orleans.

KNOTTED HAIRS (TRICHONODOSIS). F. RONCHESE, Ann. dermat. et syph. 86:41-42 (Jan.-Feb.) 1959.

Knotting of the hairs, a rather uncommon phenomenon, is not a disease, because it exists without alteration of structure. In consequence trichonodosis, noduli laqueati, trichonodosis laqueata, Haarknoten Krankheit are exaggerated and unjustified terms. It is a purely mechanical phenomenon of friction due to brushing or rolling the hairs, induced by stress. There is an interesting illustration of a figure-of-eight knot in a vulvar hair, obtained from a patient with anovulvar pruritus.

DERBES, New Orleans.

SUBACUTE NODULAR MIGRATORY PANNICULITIS. X. VILANOVA and J. NIÑOL AGUADÉ, Brit. J. Dermat. 71:45 (Feb.) 1959.

Nineteen new patients (one male) were added to the entity described in 1956 by the authors. The condition is often preceded by a sore throat and manifests as deep-seated nodules on the lower part of the legs, enlarging by confluence or peripheral extension to form plaques up to 20 cm. in diameter. The clinical and histological features lead to confusion with nodular vasculitis, Pfeiffer-Weber-Christian panniculitis, erythema nodosum, stasis cellulitis, foreign body, or tuberculoid granuloma. Potassium iodide therapy is the treatment of choice.

LAZAR, Chicago.

REACTION OF LUPUS ERYTHEMATOSUS SERUM WITH NUCLEI OF CIRCULATING AND NON-CIRCULATING CELLS. W. R. M. ALEXANDER and J. J. R. DUTHIE, Brit. M. J. 2:1565 (Dec. 27) 1958.

Coon's fluorescent antibody technique was used to confirm that sera from patients suffering from disseminated lupus erythematosus contain a globulin which combines with nuclei of tissue cells and leukocytes. The leukocytes from healthy persons showed the greatest affinity for the specific globulin.

LAZAR, Chicago.

ACNE NECROTICA DUE TO PHENYLBUTAZONE. G. A. HUNTER, Brit. M. J. 1:113 (Jan. 10) 1959.

Acne necrotica was described and illustrated in a case of a man taking phenylbutazone. Stopping the drug resulted in a remission for two months, after which reintroduction of the drug was followed by recurrence of the eruption in three weeks. The eruption cleared once again when the drug was withdrawn.

LAZAR, Chicago.

SJÖGREN'S SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS. J. H. HEATON, Brit. M. J. 1:466 (Feb. 21) 1959.

Of 28 patients with Sjögren's syndrome, 10 had L. E. cells in the peripheral blood. Two patients had Mikulicz's disease and one Felty's syndrome. Similarities between lymphadenoid goiter and Sjögren's syndrome were also noted in that middle-aged women are affected and exacerbations and remissions are present. In addition, the E. S. R. is often raised, the γ-globulin increased, and flocculation tests abnormal. Even histologic features of the diseases are similar. The author believes that Sjögren's syndrome is a form of systemic L. E. and may have etiologic factors in common with lymphadenoid goiter.

LAZAR, Chicago.

EFFECT OF INTRA-ARTERIALLY ADMINISTERED NICOTINE ON THE BLOOD FLOW IN THE HAND. B. C. R. STRÖMBLAD, Brit. M. J. 1:484 (Feb. 21) 1959.

Nicotine caused vasoconstriction in the hand when injected in the brachial artery. The amount absorbed during smoking would be enough to cause vasoconstriction via a local mechanism.

LAZAR, Chicago.

PURPURA MAJOCCHI. R. CAVALIERI, Cronache dell'I. D. I. 13:114-123 (June) 1958.

In two cases of purpura Majocchi, temporary improvement was obtained by prednisone therapy.

RONCHESE, Providence, R. I.

ETIOPATHOGENESIS OF ECZEMA. C. SCARPA, Folia allergol. 4:229-290, 1957.

A study of over a thousand cases of eczematoid dermatitis with emphasis on the importance of the combination of many factors—chemicals, fungi, pyogenes, food, pollens, and dusts in its development.

RONCHESE, Providence, R. I.

ADVANTAGES OF POLARIZED-LIGHT MICROSCOPE IN THE STUDY OF HUMAN SKIN. V. A. PUCCINELLI, Gior. ital. Dermat. e sif. 99:8-39 (Jan.-Feb.) 1958.

A well-illustrated study of epidermal structures with polarized-light microscope.

RONCHESE, Providence, R. I.

IMMUNO-BIOLOGIC STUDIES IN COLLAGEN DISEASES. L. RASPONI, Gior. ital. dermat. e sif. 99:113-126 (March-April) 1958.

Rasponi found cryoglobulinemia in 1 case of lupus erythematosus chronic discoid in a group of 22 cases examined; in all 7 cases investigated of systemic lupus erythematosus, in 1 of 2 cases of generalized scleroderma and none in 4 cases of circumscribed scleroderma.

RONCHESE, Providence, R. I.

NAIL CHANGES IN PSORIASIS. L. NARDELLI, Gior. ital. dermat. e sif. 99:257-268 (May-June) 1958.

True ungual psoriasis is separated from atypical manifestations bearing similarities, for instance, with onychomycosis. The nail is involved in psoriasis because it is an epidermal product, while the hair remains unaffected because it is more directly related to the dermal papilla.

RONCHESE, Providence, R. I.

A STUDY OF TWENTY-FIVE SYPHILITIC CHANCRES OBSERVED BETWEEN JANUARY 1957, and APRIL, 1958. F. SEBASTIANI, Gior. ital. dermat. e sif. 99:341-345 (July-Aug.) 1958.

The cases were observed in a community of about 100,000 inhabitants. Some had a herpetic appearance; others were impetiginous; others were dyphteroid and three were necrotic. Of interest were the atypical morphology and the discordant serology.

RONCHESE, Providence, R. I.

DERMATOSES OF RICE WORKERS. F. GIANOTTI and R. LUVONI, Gior. ital. dermat. e sif. 99:377-405 (Sept.-Oct.) 1958.

A well-documented investigation on the dermatoses affecting the workers in the rice fields, due to 12 different types of cercariae.

RONCHESE, Providence, R. I.

THE REGROWTH OF HAIR IN ALOPECIA AREATA AND MALIGNA FOLLOWING INTRACUTANEOUS INJECTIONS OF HYDROCORTISONE. K. W. KALKOFF and E. MACHER, Hautarzt 9:441-451 (Oct.) 1958.

Intracutaneous injections of hydrocortisone into lesions of alopecia areata or alopecia totalis will cause regrowth of pigmented hair of normal thickness at the site of the injection within three to five weeks. This course of events differs from the pattern of spontaneous regrowth. Histologically, the characteristic lymphocytic infiltrate in the papilla and around the bulbus disappears, and new pigment is formed in the matrix. Contrariwise, cases of atrophic or premature alopecia treated in the same manner do not show regrowth of hair. The practical value of this type of treatment is limited, since a recurrent loss of hair in the treated field must be excepted when the effect of the hydrocortisone has worn off.

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RETICULUM CELL SARCOMATOSIS COMPLICATING ACRODERMATITIS CHRONICA ATROPHICANS: SERUM PROTEIN STUDIES IN RETICULO-HISTIOCYTIC NEOPLASMA OF THE SKIN. W. KNOTH, Hautarzt 9:456-460 (Oct.) 1958.

Two cases are reported of reticulum-cell sarcomatosis occurring as a complication of acrodermatitis chronica atrophicans. Paper-electrophoretic testing of the serum proteins showed a tendency to reversal of the A/G ratio. These findings are considered to be of prognostic value. In an additional case of a solitary reticuloma, for example, the γ-globulin was also increased, which suggests that this lesion might be the first manifestation of a future reticulum-cell sarcomatosis.

BULEY, Champaign, Ill.

AN ADDITIONAL CASE OF ICHTHYOSIS LINEARIS CIRCUMFLEXA. M. MANOK, Hautarzt. 9:461-463 (Oct.) 1958.

A rare variety of congenital ichthyosis, first described by Comèl under the name of ichthyosis linearis circumflexa, is reported. Although a low vitamin A level was found in the blood, treatment with high doses of vitamin A resulted in only a slight improvement of the dermatosis.

BULEY, Champaign, Ill.

THE HISTIOGENESIS OF CHONDRO-DERMATITIS NODULARIS HELICIS (WINKLER). J. J. HERZBERG, Hautarzt 9:494-500 (Nov.) 1958.

The histological sections of 42 cases of chondrodermatitis nodularis helicis are reviewed in the light of previously advanced concepts of the pathogenesis of the disease. The author concludes that the disease process consists of a proliferation of perichondrial cells, reticulum fibers, and a cartilage-like ground substance which, together, represent an incompletely differentiated cartilaginous tissue.

BULEY, Champaign, Ill.

PANNICULITIS NODULARIS NONSUPPURATIVE. O. FRESEN, Hautarzt 9:500-503 (Nov.) 1958.

Two cases of nonsuppurative nodular panniculitis are reported. The tendency of the disease to recur and the histological changes suggest that nonsuppurative panniculitis is an allergic sensitization reaction to various noxae. The process is not necessarily limited to the skin. An initial vasculitis leads to necrosis of fat tissue and consequent formation of nonspecific granulomas.

BULEY, Champaign, Ill.

THE SERUM PROTEINS IN LIPOID PROTEINOSIS (URBACH-WIETHE). C. EBERHARTINGER and F. REINHARDT, Hautarzt 9:503-507 (Nov.) 1958.

The serum protein findings in a case of lipoid proteinosis are reported. There was a reversal of the A/G ratio with an increase in the α- and γ-globulin fractions. There was also an increase in the phospholipids, while the cholesterol content in the serum was normal. The ultracentrifuge analysis showed a marked increase in the total lipoproteins. By comparing the electrophoretic patterns before and after the treatment of the serum in the ultracentrifuge, it could be demonstrated that the increase in the α-globulins was due to that in the lipoprotein fraction.

BULEY, Champaign, Ill.

ELECTROPHORETIC ANALYSIS OF THE GLYCOPROTEINS IN SERUM AND BLISTER CONTENT AFTER PHYSICAL IRRITATION OF THE SKIN. A. MONTAGNANI and A. R. COFANO, Hautarzt 9:507-510 (Nov.) 1958

Before and after irradiation of the skin with soft x-rays, the proteins and glycoproteins in the blood serum and in cantharides blister fluid were determined. After irradiation, an increase of proteins was observed in the blood, while in the blister fluid, after an initial decrease of all protein fractions, the findings returned to the normal values. In nonirradiated blisters, the glycoprotein was augmented, and it appeared, therefore, that irradiation checked such change.

BULEY, Champaign, Ill.

ANATOMICAL AND PHYSIOLOGICAL ASPECTS OF GASTRIC MUCOSA IN DERMATOSES. G. MORETTI and R. CHELI, Minerva dermat. 33:247-251 (June) 1958.

The secretion and the histology of the gastric mucosa were studied by biopsy in 36 patients. Abnormalities were found in the cases in which there was a gastric disorder. No abnormality could be considered characteristic of a dermatosis.

RONCHESE, Providence, R. I.

EPITHELIOMA DEVELOPED AFTER USE OF TAR FOR PRURITUS. G. CARLI, Minerva dermat. 33:280-281 (July) 1958.

A squamous-cell epithelioma developed on the vulva of a 64-year-old woman after the use of a tar ointment for six months.

RONCHESE, Providence, R. I.

CUTANEOUS HEMANGIOMA AND HEMANGIOMATOSIS. D. ROSSELLI, Minerva dermat. 33:381-472 (Nov.) 1958.

An extensive and well-illustrated study on history, classification, etiopathogenesis and therapy based on 2,000 personal cases. Spontaneous involution is practically not mentioned.

RONCHESE, Providence, R. I.

DEMONSTRATION OF PLATELETS LYSIS IN THROMBOCYTOPENIC PURPURA IN A CASE OF SYSTEMIC LUPUS ERYTHEMATOSUS. M. TAMPONI, Minerva dermat. 33:473-481 (Dec.) 1958.

A report of thrombocytopenic purpura developing in a case of systemic lupus erythematosus. A platelet lytic factor and its disappearance with the purpura after splenectomy are discussed. The patient remained well four years after the operation.

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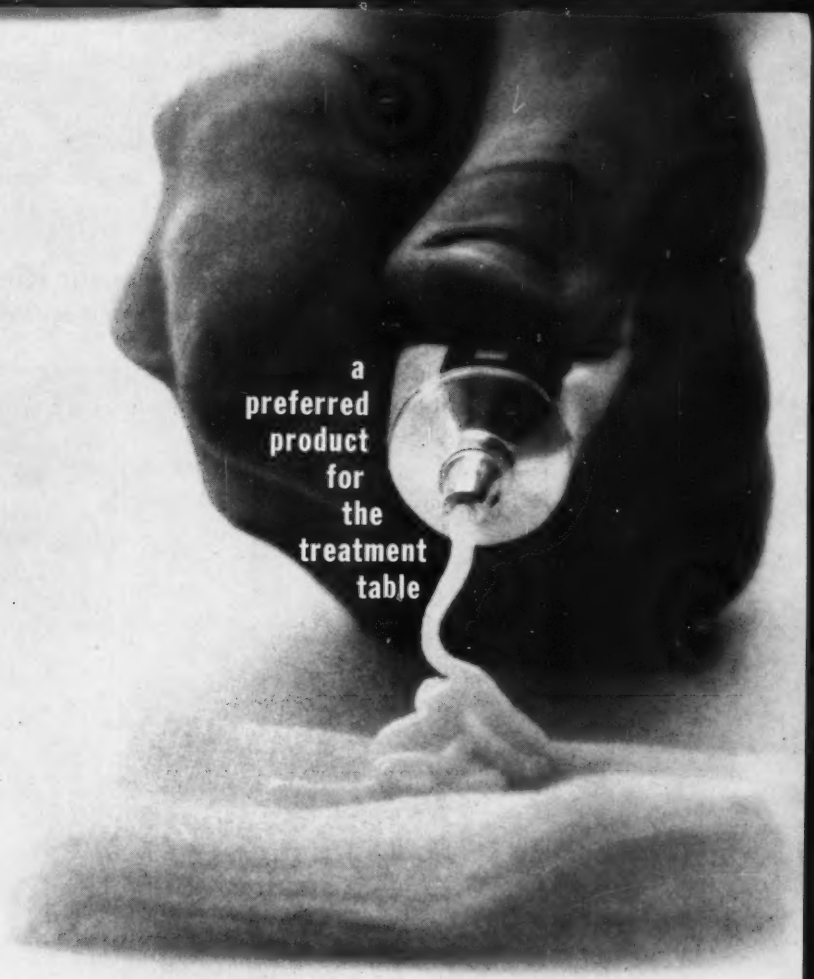

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Reference: Gross E. R. and Wright C. S., A. M. A. Archives of Dermatology, 78:92, July, 1958

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Burke, J. F., and Golden, T.:
Am. J. Surg. **95**:828, 1958.

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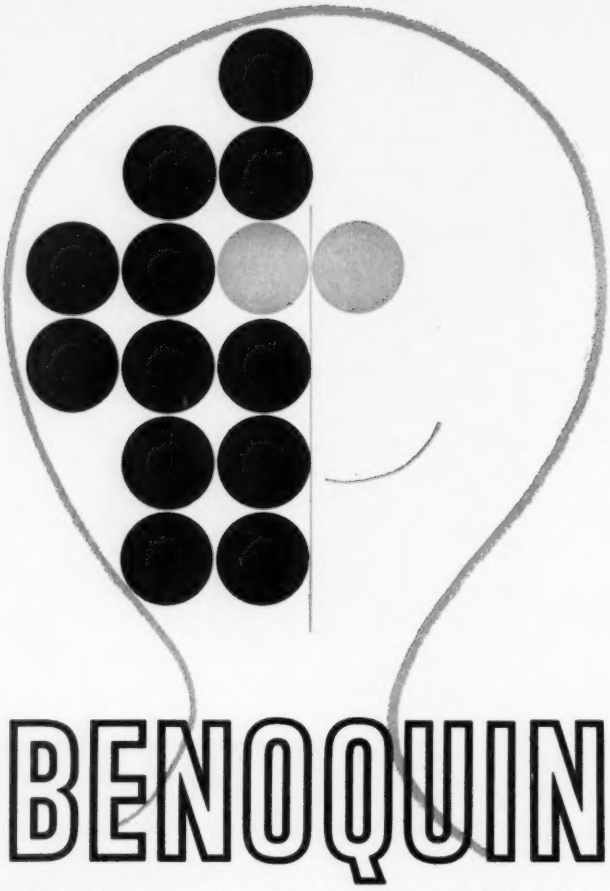

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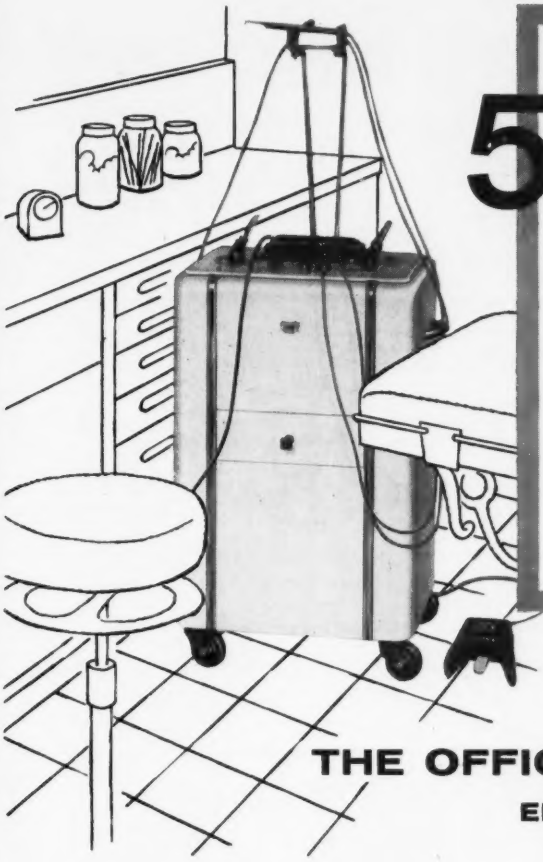

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Mount Vernon, N.Y.

- effective wound cleansing and healing
- well tolerated and convenient for outpatient use
- economical for hospital and patient

PANAFIL ointment (papain – urea – water-soluble chlorophyll derivatives) • For complete information see your Physicians' Desk Reference
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Pleasingly and efficiently
serving patient and physician
during all seasons

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BASIS® SOAP

For dry sensitive skin
Available at Prescription Pharmacies

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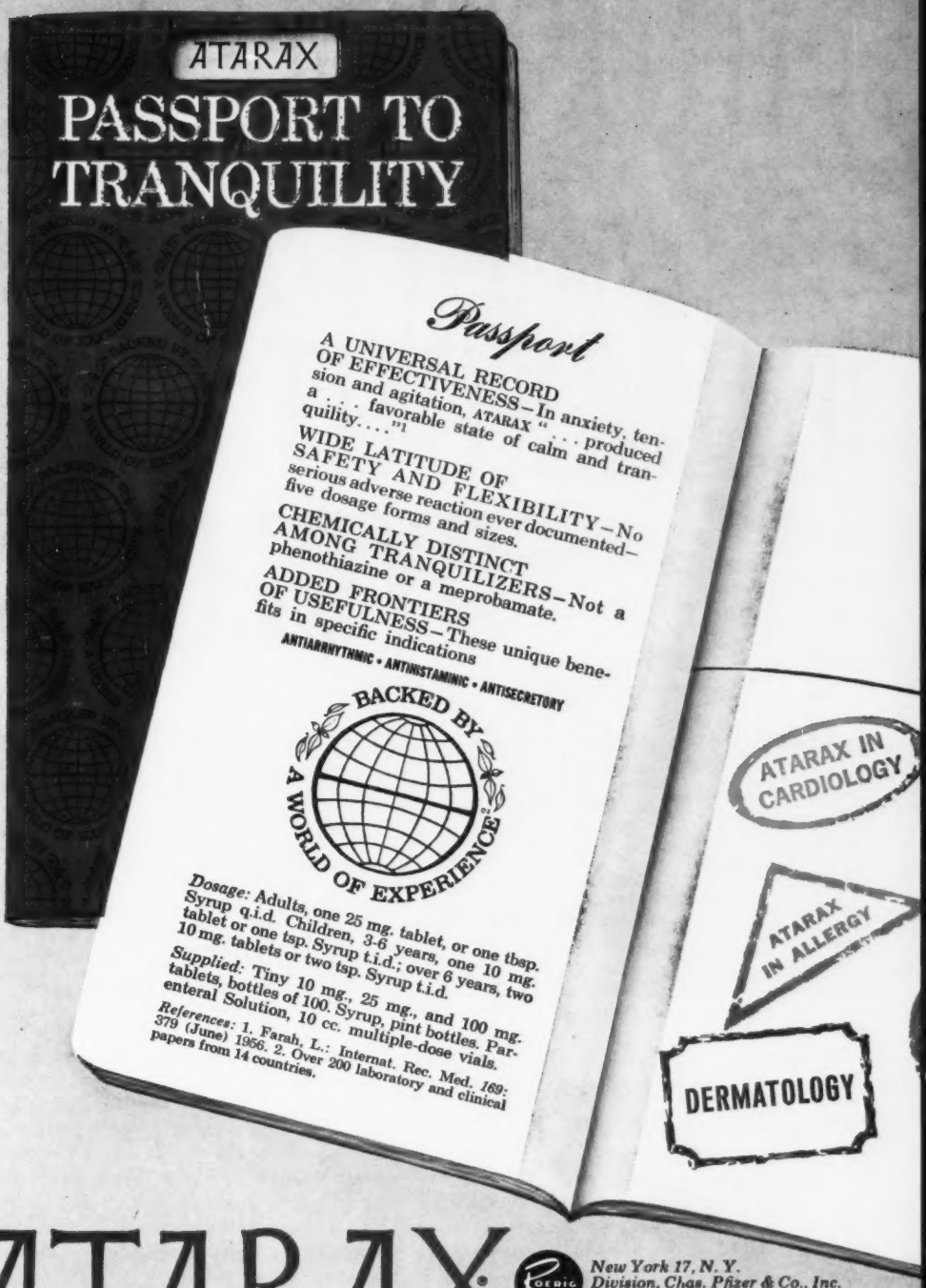
SOUTH NORWALK, CONN., U.S.A.

Mfrs. of Aquaphor®—Elastoplast®


ATARAX
PASSPORT TO TRANQUILITY
Passport
A UNIVERSAL RECORD OF EFFECTIVENESS—In anxiety, tension and agitation, ATARAX "... produced a ... favorable state of calm and tranquility...."[1]
WIDE LATITUDE OF SAFETY AND FLEXIBILITY—No serious adverse reaction ever documented—five dosage forms and sizes.
CHEMICALLY DISTINCT AMONG TRANQUILIZERS—Not a phenothiazine or a meprobamate.
ADDED FRONTIERS OF USEFULNESS—These unique benefits in specific indications
ANTIARRHYTHMIC • ANTIHISTAMINIC • ANTISECRETORY
BACKED BY A WORLD OF EXPERIENCE
Dosage: Adults, one 25 mg. tablet, or one tbsp. Syrup q.i.d. Children, 3-6 years, one 10 mg. tablet or one tsp. Syrup t.i.d.; over 6 years, two 10 mg. tablets or two tsp. Syrup t.i.d.
Supplied: Tiny 10 mg., 25 mg., and 100 mg. tablets, bottles of 100. Syrup, pint bottles. Parenteral Solution, 10 cc. multiple-dose vials.
References: 1. Farah, L.: Internat. Rec. Med. 169: 379 (June) 1956. 2. Over 200 laboratory and clinical papers from 14 countries.
ATARAX IN CARDIOLOGY
ATARAX IN ALLERGY
DERMATOLOGY

ATARAX®

(brand of hydroxyzine)

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New York 17, N. Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being

UNEXCELLED PATIENT COMFORT and safety with DYCLONE™

dyclonine hydrochloride

an unsurpassed topical anesthetic

for
instrumentations
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DYCLONE is a well tolerated topical anesthetic which is

fast-acting
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antibacterial
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virtually nonsensitizing

supply...Dyclone Creme, tubes of 1 oz. with rectal applicator. Dyclone Solution, bottles of 1 and 8 oz.

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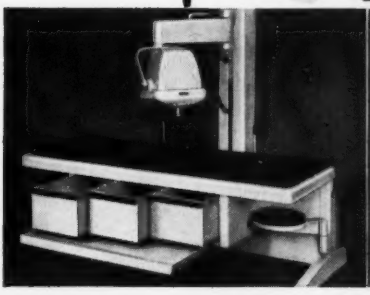
DIVISION OF ALLIED LABORATORIES, INC.
INDIANAPOLIS 6, INDIANA

superficial therapy

...*truly skin deep*

G-E MAXIMAR®100
multiplies soft-ray output — up to 84% absorption in first 4 mm of tissue; dose rates above 5000 r/m at 15-cm fsd, above 1200 r/m at 30-cm fsd



ARM'S-REACH CONVENIENCE FOR EVERYTHING YOU NEED...

Comfortably cushioned table — includes swing-out treatment seat . . . drawer for *flat storage* of lead-rubber sheeting . . . bins for all accessories.

Those times when *skin deep* is exactly *deep enough* — that's when you'll truly appreciate your Maximar 100. Foremost reason is its exclusive Coolidge tube with beryllium window: soft rays exit *in quantity* — are not filtered out as they would be with other materials. So Maximar 100's range easily extends from output approaching grenz rays to the depth penetration obtained at 100 kvp. Control is precise . . . dosage exact. And coverage at 30-cm focal/skin distance will span at least an 18-cm circle — perimeter output remaining at least at 80% of full center strength on an 18-cm circle! Talk over details of the Maximar 100 soon with your G-E x-ray representative. Or write X-Ray Department, General Electric Company, Milwaukee 1, Wisconsin, for illustrated Pub. P-92.

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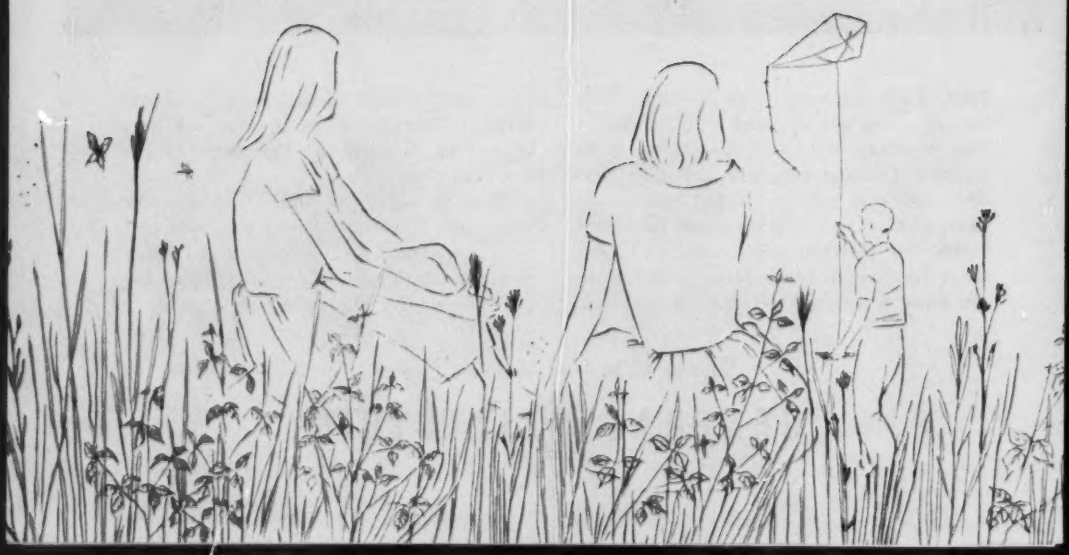
COVER THE
SUMMER FRONT...
WITH THREE
HIGHLY EFFECTIVE
CORTICOSTEROID
TOPICALS



INFLAMMATORY AND ALLERGIC SKIN CONDITIONS

Aristocort® *CREAM*

Triamcinolone Acetonide 0.1%
TUBES OF 5 GM. AND 15 GM.

Aristocort® *OINTMENT*

Triamcinolone Acetonide 0.1%
TUBES OF 5 GM. AND 15 GM.

INFLAMMATORY, ALLERGIC, INFECTIVE EYE AND EAR CONDITIONS

Neo-Aristocort®

Neomycin-Triamcinolone Acetonide 0.1%
TUBES OF ⅛ OZ.

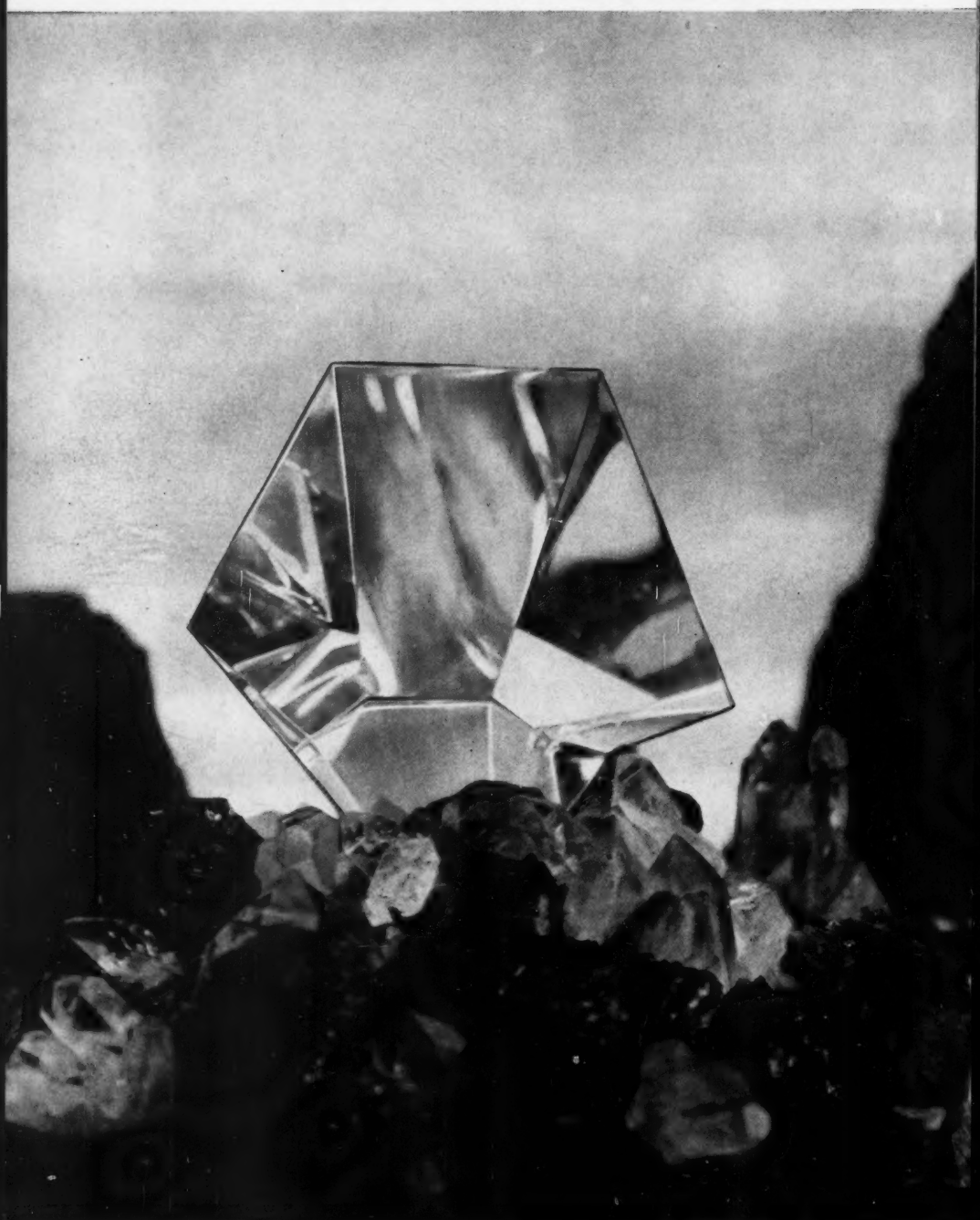
EYE-EAR OINTMENT

Each, sparingly applied, offers the unsurpassed efficacy of ARISTOCORT in topical situations...with 10-fold the potency of hydrocortisone topically yet *without* the hazards associated with systemic absorption

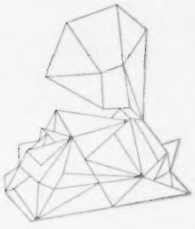
Lederle

LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

PURE ANTIHISTAMINE ACTION
A PHARMACOLOGIC FACT
BECAUSE DĪSOMER
SHEDS THE MOLECULAR DROSS



NEW...IN THE TREATMENT OF ALLERGIC DISORDERS



- *"...high therapeutic index"*[1]
- *unsurpassed clinical efficacy*
- *highly effective in exceptionally small doses*
- *side effects reduced to minimal level*

Disomer....a scientific contribution in the pharmacology of antihistamines!

Incorporating the newest knowledge of structure-function relationships, DISOMER comes close to the therapeutic ideal of pure antihistamine activity. DISOMER represents the *d*-isomer of racemic brompheniramine maleate. In shedding the *l*-isomer a high point in clinical effectiveness is achieved while side effects are reduced to a minimal level.

Therapeutic results have been noteworthy with 94.7% effectiveness reported.[2] Equally noteworthy is the low incidence of clinically significant adverse reactions. Indeed, the sole side effect reported was occasional, mild drowsiness in only 4.7% of patients.

With DISOMER your allergic patient remains your alert patient while enjoying unsurpassed freedom from allergic symptoms. Ready now for your prescription—DISOMER is available in a variety of dosage forms to fit your patients' individual requirements.

Availability:

DISOMER CHRONOTAB*	6 mg.
DISOMER CHRONOTAB*	4 mg.
DISOMER Tablets	2 mg.
DISOMER Syrup	2 mg. per 5 cc.

Usual dosage:

6 mg. CHRONOTAB	b.i.d.
4 mg. CHRONOTAB	t.i.d.
2 mg. Tablet	q.i.d.
Syrup 1 teaspoonful	q.i.d.

**Chronotab* *is White's repeat-action tablet.*

References: (1) Gould, A. H. and Long, D. L.: Clinical Pharmacology and Therapeutic Use of Dexbrompheniramine Maleate (Disomer), a new Histamine Antagonist (submitted for publication). (2) Medical Department, White Laboratories, Inc.

WHITE LABORATORIES, INC.
Kenilworth, New Jersey

DISOMER

DEXBROMPHENIRAMINE MALEATE

...sheds the molecular dross

DISPERSE!

A military tactic is added to the dermatologist's armamentarium

American rebels taught British Redcoats the value of dispersing during the Revolutionary War. This deployment increased the area one man could cover effectively—while decreasing the risk. By dispersing their troops, the shrewd Yankees successfully harried the rigidly maintained columns of King's Regulars at every turn.

Medical science has borrowed this tactic of dispersion to make safer the use of one of dermatology's most effective weapons—crude coal tar. Crude coal tar's usefulness is undisputed, but the high incidence of irritation resulting from its use has caused many doctors to prescribe it only sparingly, if at all.

Postulating that the large tar particle size (up to 100 microns) in crude coal tar could be partially responsible for the irritation, Pflag and Zopf (1) discovered the means to reduce the tar particles to about 3 microns. Further reasoning led Carney and Zopf (2) to believe that a lower concentration of this minutely dispersed coal tar would be as effective as the commonly prescribed 2% to 5% preparations of ordinary tar. Clinical studies upheld their theory. Thus, the dispersion of the smaller tar particle size in a lower concentration resulted in a greatly lowered incidence of irritation without diminution of its therapeutic effectiveness —indeed an important addition to the dermatologist's armamentarium.

Dispertar Ointment, made according to the Carney and Zopf method, provides 1% coal tar and 0.5% polyoxyethylene sorbitan monolaurate (solutar) in an oleaginous base which adheres well to the skin, protects against chemical and mechanical trauma, is occlusive and gives some lubrication. Tests prove Dispertar Ointment may be prescribed freely and the trend is to its use on active, acute dermatitis.

For more detailed information and sample of

DISPERTAR OINTMENT

write to:

TEXAS PHARMACAL COMPANY

San Antonio, Texas

IN CANADA—Omega Laboratories, Ltd., Montreal and Toronto

1. Pflag, S.C. and Zopf, L.C.; Hydrophilic Forms of Tars, *U. S. Armed Forces M. J.* 2:1177-1181 (Aug.) 1951.

2. Carney, R.G. and Zopf, L.C.; An Improved Coal Tar Ointment Using a Surfactant, *Arch. of Dermat.* 72:266-271 (Sept.) 1955.

For the treatment of dry, scaly skin

LOWILA EMOLLIENT

an effective skin moisturizer

moisturizes and softens the skin

promotes moisture retention

supplements natural skin oils

restores and maintains normal skin pH

Lowila Emollient hydrates the skin . . . keeps it soft and smooth

Lowila Emollient is a new, effective skin moisturizer for the treatment of dry, scaly skin. It contains an excellent keratin-moisturizing agent Kerohydric®, a crystal-clear, dewaxed oil-soluble fraction derived from lanolin.

Lowila Emollient moisturizes the skin and promotes retention of moisture. When applied to the skin, Lowila Emollient provides a partially-occlusive "breathing" film that: (1) supplies its own water to the dehydrated keratin layer, (2) prevents excessive evaporation when the atmosphere is dry, (3) allows the skin to absorb water from an atmosphere with normal humidity.

Lowila Emollient also supplements natural skin oils, restoring the protective action of skin lipids lost through effects of water, weather and detergents. In Lowila Emollient, Kerohydric is dispersed in a lactic acid buffered emulsion that restores and maintains normal skin acidity.

LOWILA EMOLLIENT

Indications

For dryness, flaking and scaling following therapy of acute inflammation
Dermatitis of the hands ("Housewives' eczema")
In chronic atopic dermatitis
Pruritus senilis—pruritus hiemalis
In nummular dermatitis
In psoriasis
Xerosis or asteatosis
Sunburn
Diaper rash
Chafed or chapped skin
Ichthyosis

Caution: Lowila Emollient is partially occlusive. Therefore it should not be used until the skin is free of inflammation.

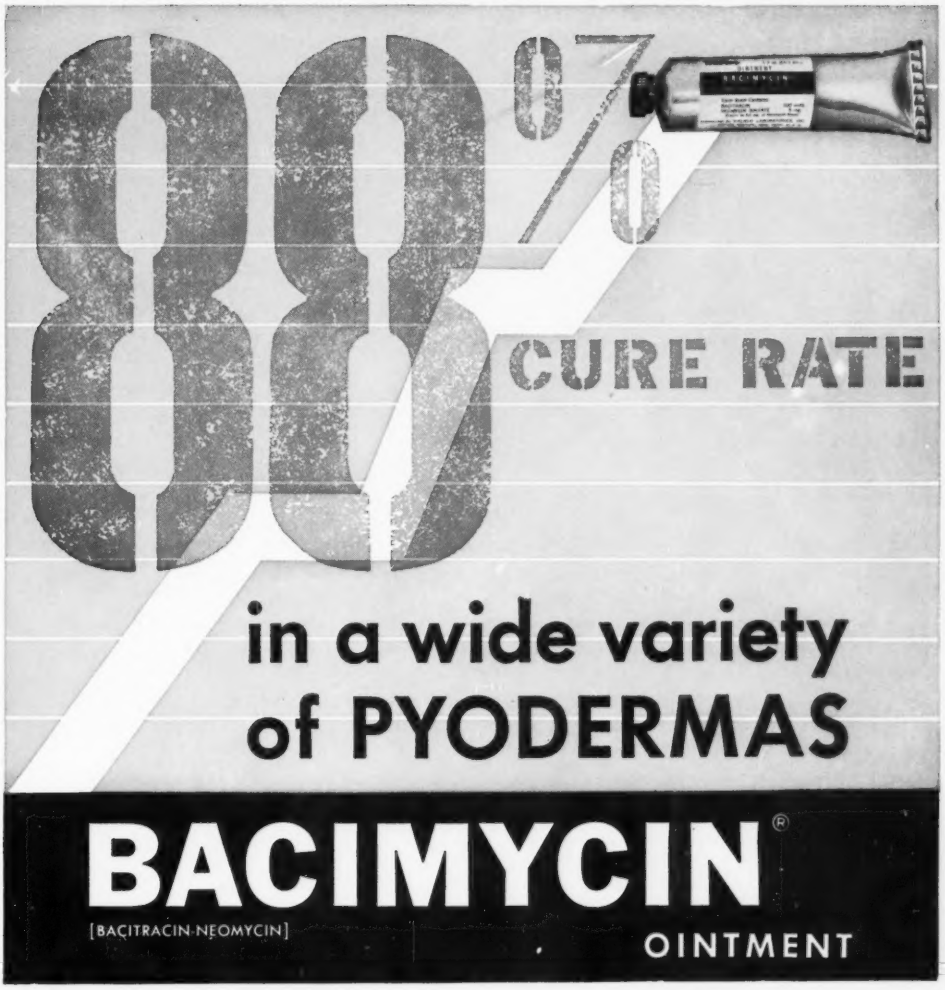
Application:

Gently rub a small amount into affected areas three or more times a day and at bedtime. Use particularly after exposure to water, soap and detergents.

Availability:

Lowila Emollient is supplied in 62.5 gram tubes.

WESTWOOD PHARMACEUTICALS
Division of Foster-Milburn Company
Buffalo 13, New York



a first choice for dual antibiotic therapy

In a recent study[1] of 53 patients with various types of pyodermas, the use of BACIMYCIN Ointment "... resulted in a cure rate of 88%...." Impetigo, infectious eczematoid dermatitis, atopic eczema, secondary infections superimposed on dermatitis venenata, and folliculitis were among the common skin infections that showed marked improvement with BACIMYCIN therapy.

BACIMYCIN rarely produces sensitization or primary irritation.

Supplied in ½ oz. tubes for prescriptions; in 100 gm. jars for hospital use; in ⅛ oz. tubes for ophthalmic use. Also supplied as BACIMYCIN with Hydrocortisone, ⅛ oz. tube with applicator tip.

Literature and samples on request.

1. Greenhouse, J. M., and Ryle, W. C.: A.M.A. Arch. Dermat. & Syph. 69:366 (March) 1954.

Walker **LABORATORIES, INC.** MOUNT VERNON, NEW YORK

spreads
THINLY · EVENLY · ECONOMICALLY
in acute dermatologic conditions

SUPERTAH® H-C

(1.25% COAL TAR FRACTION WITH HYDROCORTISONE 1%)

antiinflammatory — antipruritic

- water miscible base . . . purified white tar fraction, stainless, washable
- maximum efficiency . . . spreads thinly for evenly distributed therapeutic action and great economy
- enhanced benefits . . . more effective than either agent alone
- excellent response . . . deep penetration to source of inflammation

supplied: ½-oz. tube

also available:

SUPERTAH Ointment (1½-oz. tube)
provides the therapeutic effectiveness of time-proved tar medication

SUPERTAH S/S (with salicylic acid and sulfur; 1½-oz. tube)
for keratolytic action

All Supertah preparations are made with refined natural coal tar fraction

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